

1/31

FIG. 1

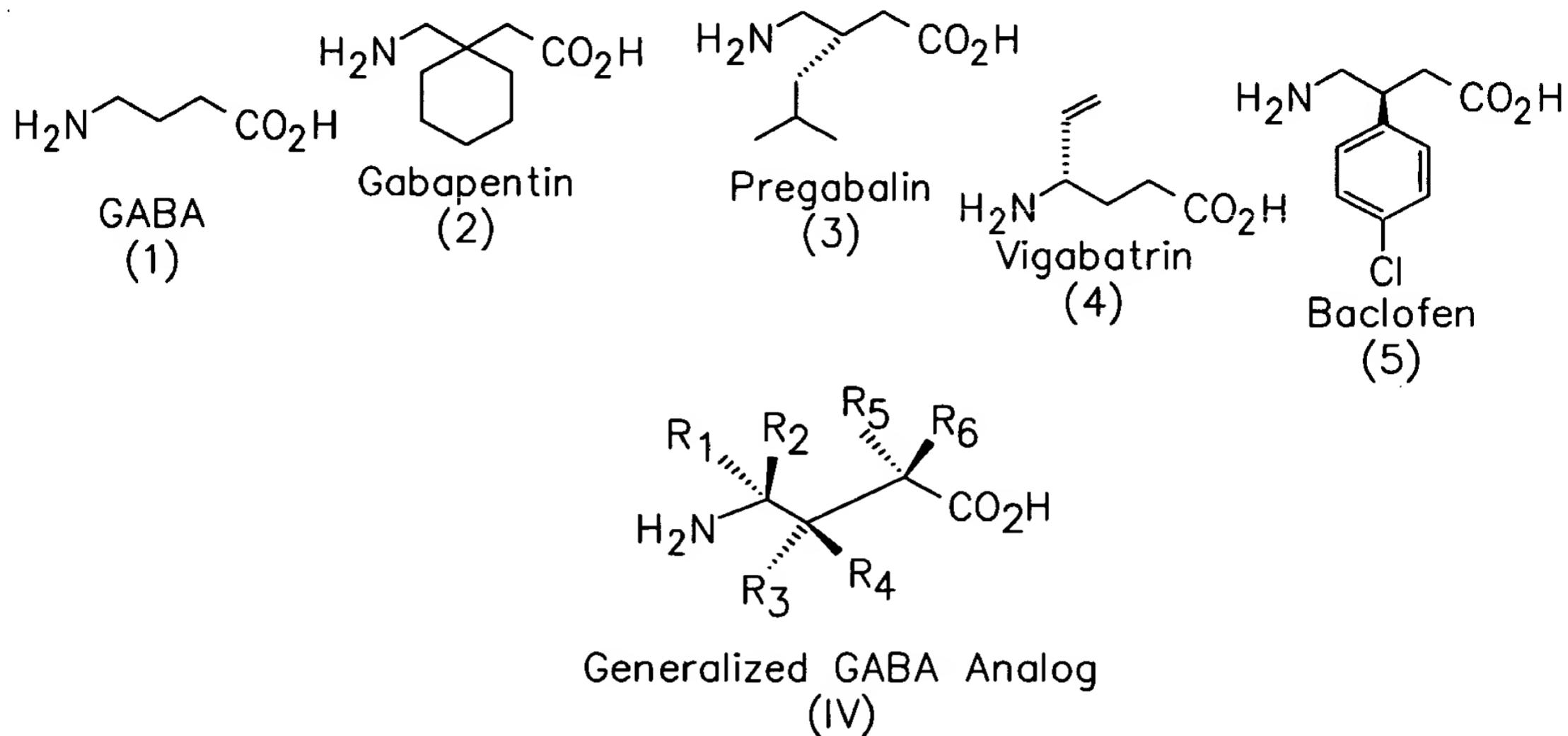
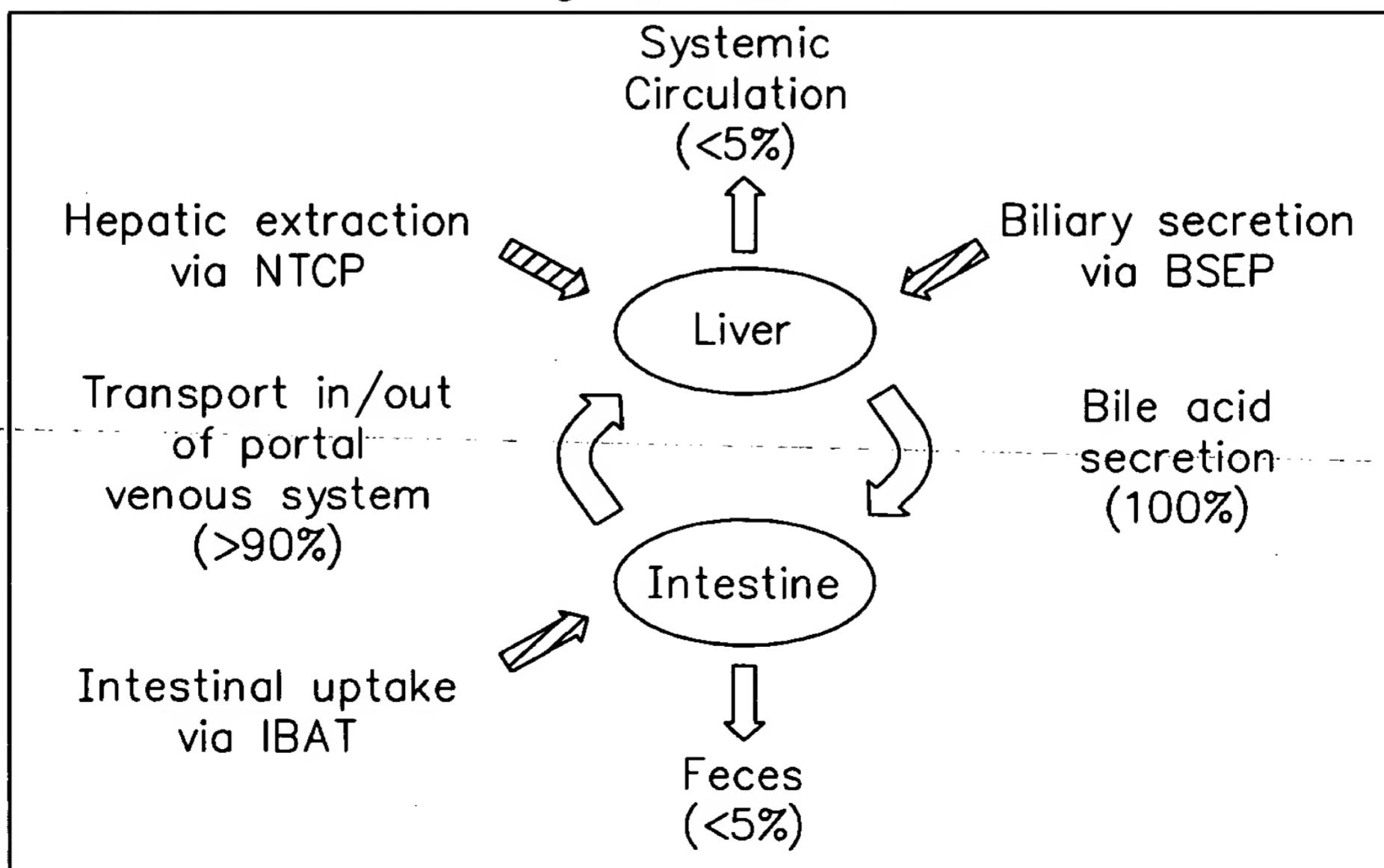


FIG. 2

The Enterohepatic Circulation with Key Transporter Proteins Mediating Bile Acid Circulation



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FIG. 3

Bile Acid Conjugates of HMG-CoA Reductase Inhibitor

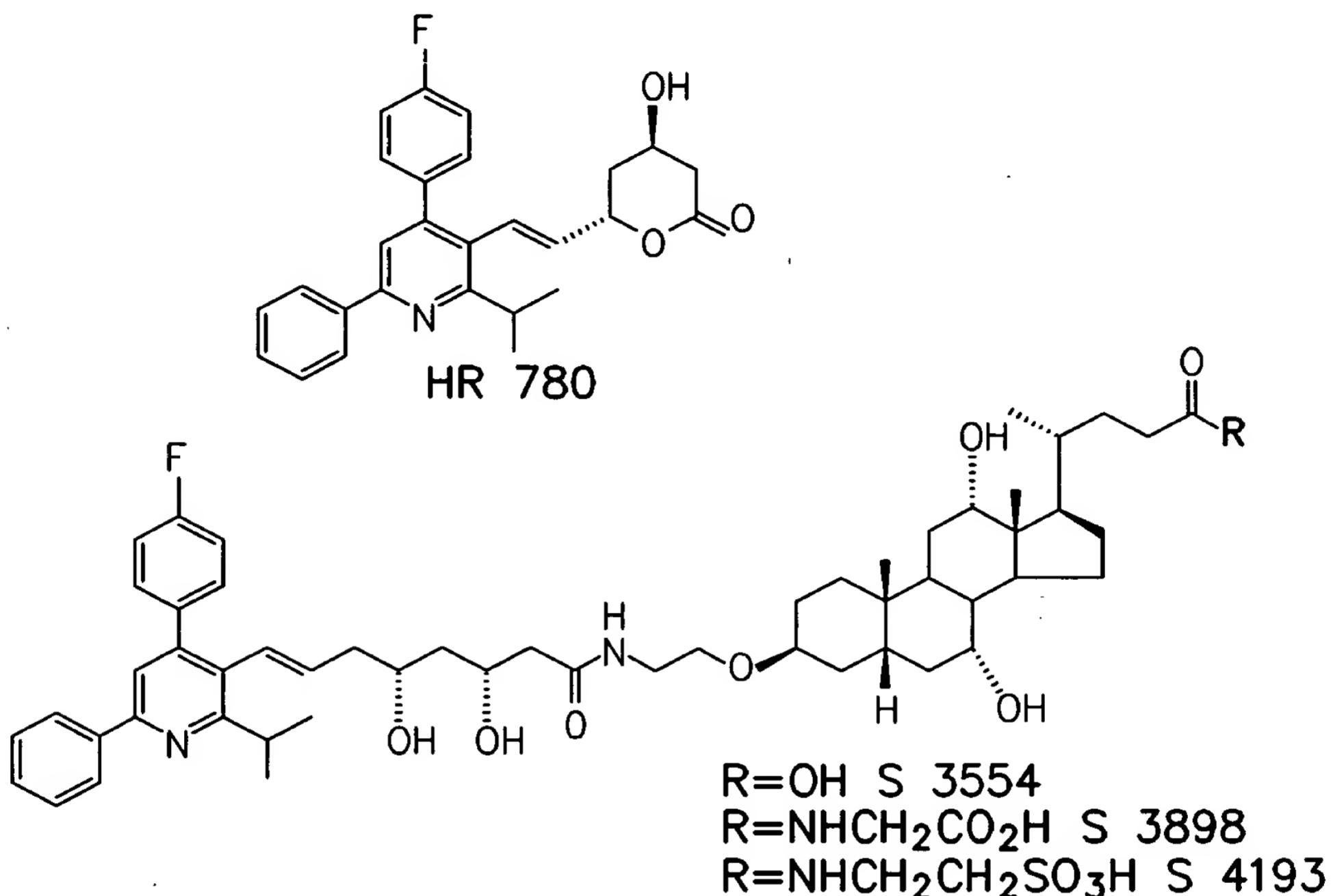
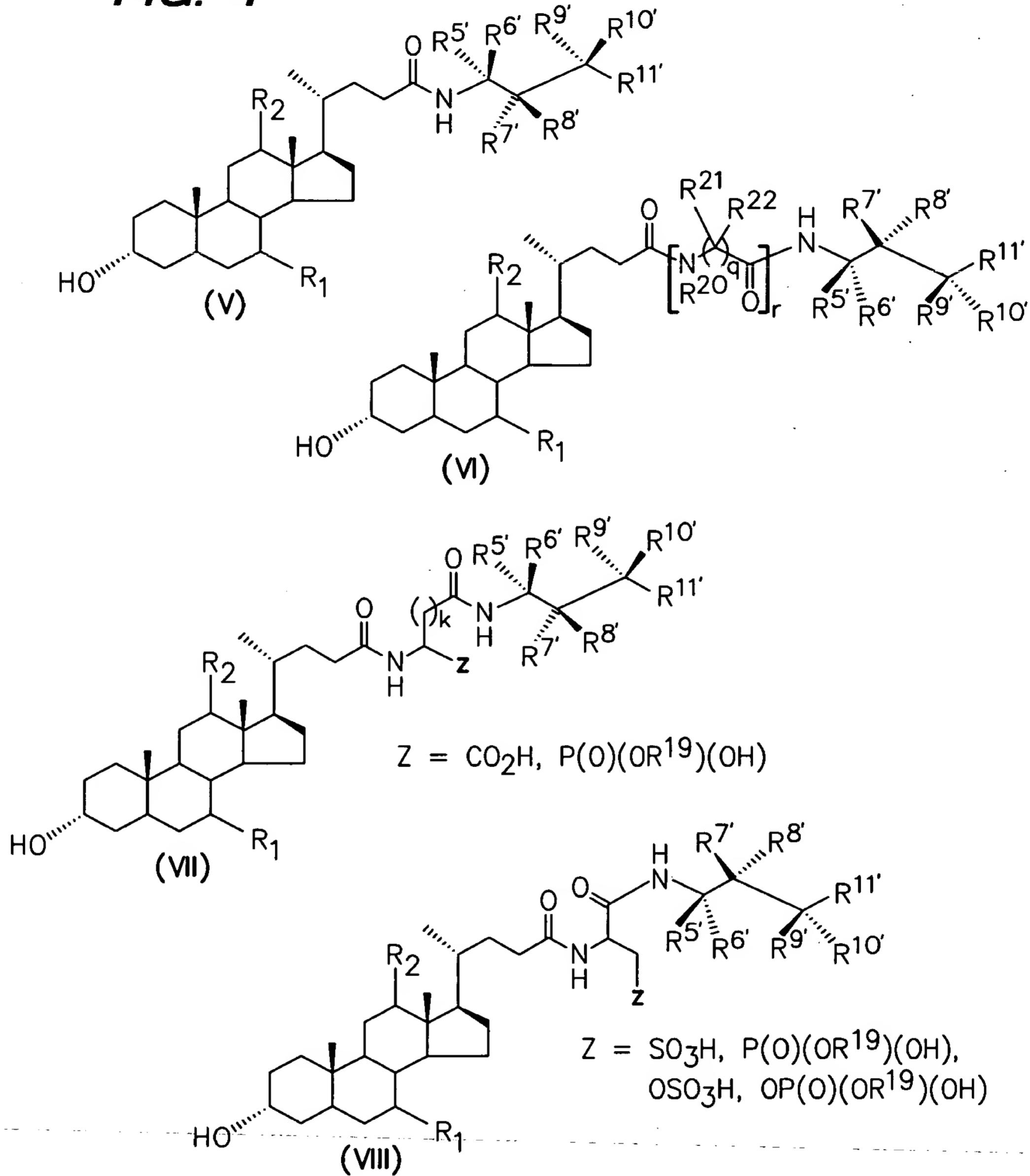


FIG. 4

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R₁ = α -OH; R₂ = α -OH (Cholate)

R₁ = β -OH; R₂ = H (Ursodeoxycholate)

R₁ = α -OH; R₂ = H (Chenodeoxycholate)

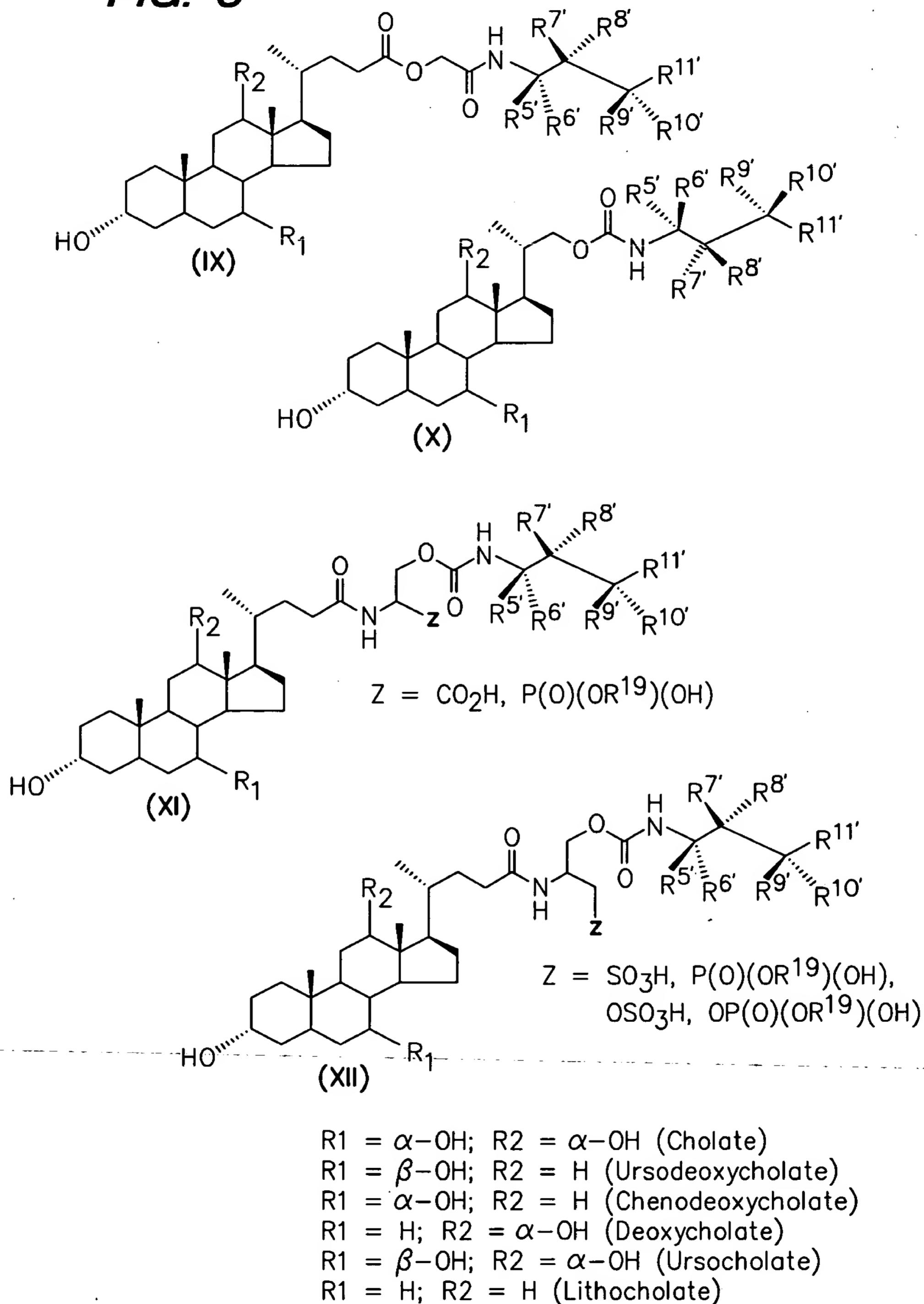
R₁ = H; R₂ = α -OH (Deoxycholate)

R₁ = β -OH; R₂ = α -OH (Ursodecholate)

R₁ = H; R₂ = H (Lithocholate)

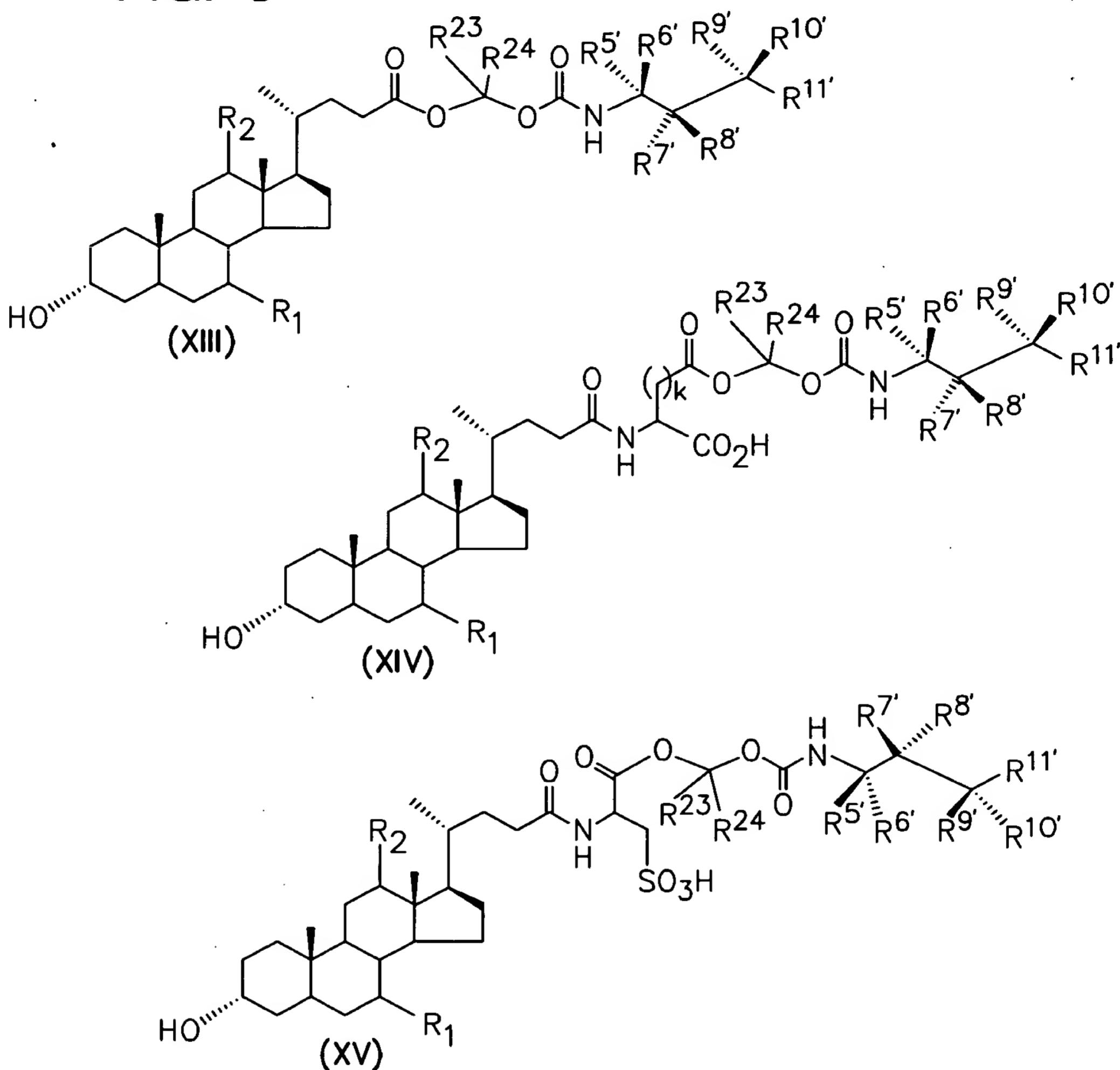
FIG. 5

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FIG. 6



R₁ = α -OH; R₂ = α -OH (Cholate)

R₁ = β -OH; R₂ = H (Ursodeoxycholate)

R₁ = α -OH; R₂ = H (Chenodeoxycholate)

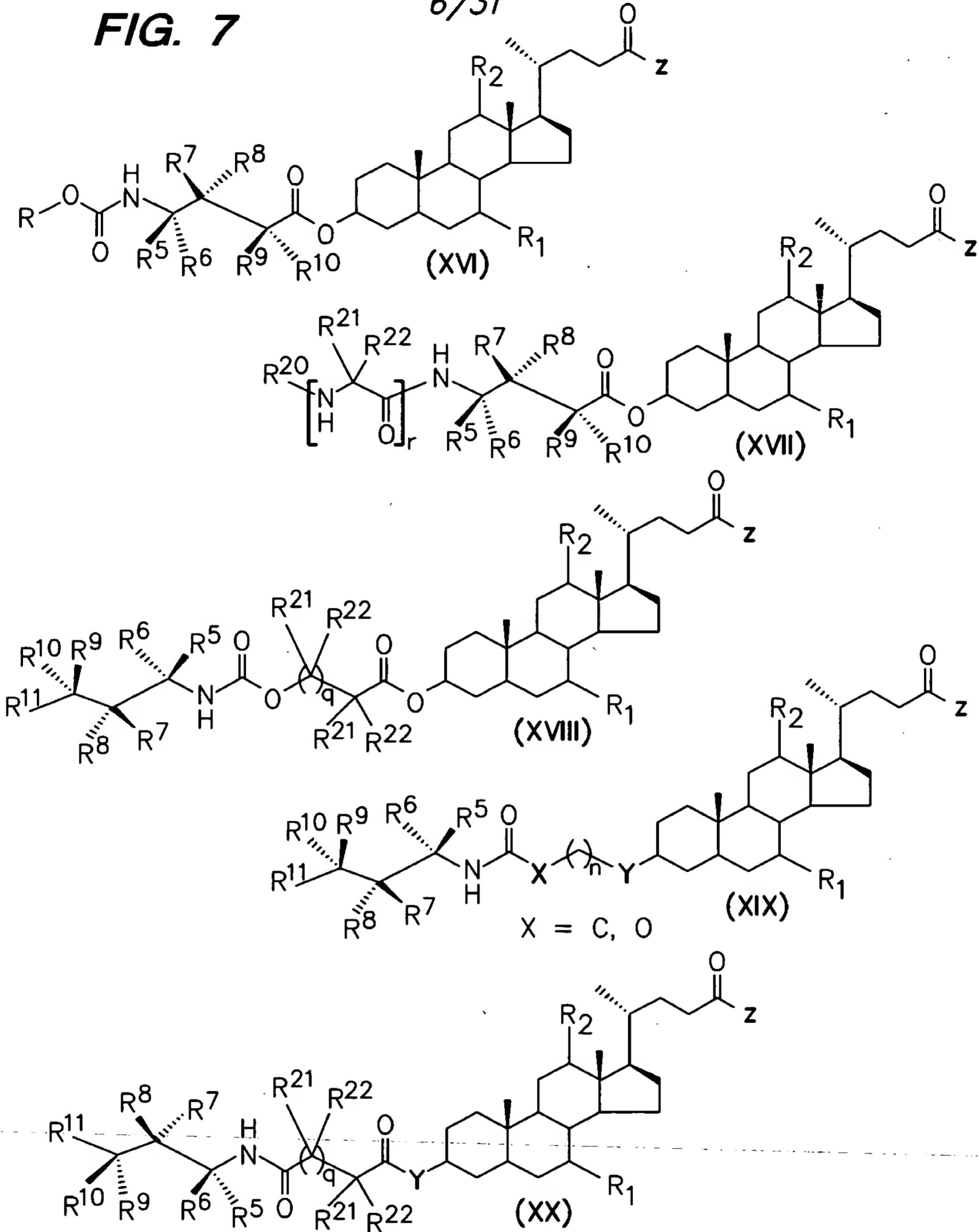
R₁ = H; R₂ = α -OH (Deoxycholate)

R₁ = β -OH; R₂ = α -OH (Ursodecholate)

R₁ = H; R₂ = H (Lithocholate)

FIG. 7

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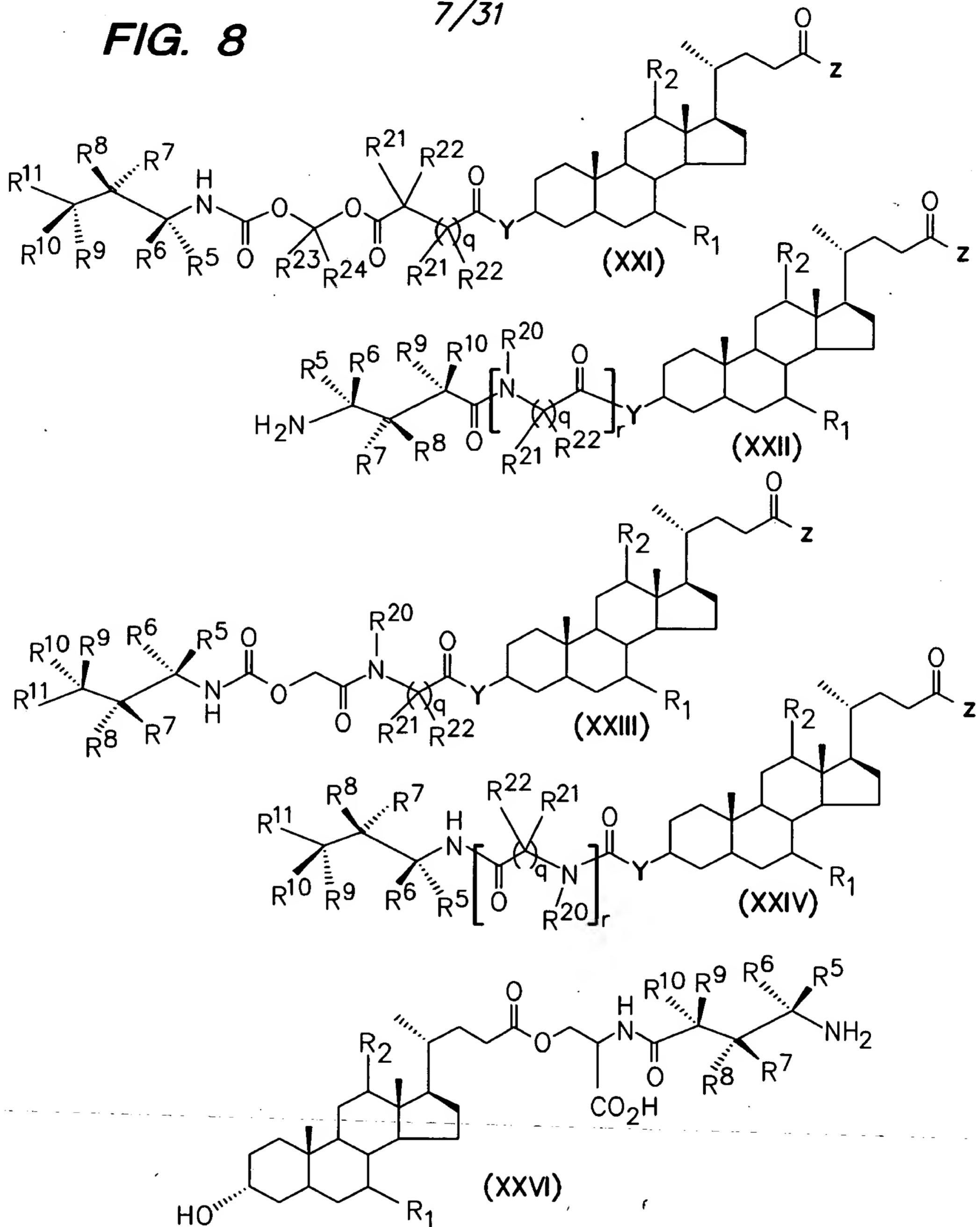
$\text{R}_1 = \alpha\text{-OH}; \text{R}_2 = \alpha\text{-OH}$ (Cholate)
 $\text{R}_1 = \beta\text{-OH}; \text{R}_2 = \text{H}$ (Ursodeoxycholate)
 $\text{R}_1 = \alpha\text{-OH}; \text{R}_2 = \text{H}$ (Chenodeoxycholate)
 $\text{R}_1 = \text{H}; \text{R}_2 = \alpha\text{-OH}$ (Deoxycholate)
 $\text{R}_1 = \beta\text{-OH}; \text{R}_2 = \alpha\text{-OH}$ (Ursocholate)
 $\text{R}_1 = \text{H}; \text{R}_2 = \text{H}$ (Lithocholate)

$\text{Y} = \alpha\text{-O}$
 $\text{Y} = \beta\text{-O}$
 $\text{Y} = \alpha\text{-NH}$
 $\text{Y} = \beta\text{-NH}$

$\text{Z} = \text{OH}$
 $\text{Z} = \text{N}(\text{H})\text{CH}_2\text{CO}_2\text{H}$
 $\text{Z} = \text{N}(\text{H})\text{CH}_2\text{SO}_3\text{H}$

FIG. 8

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$R_1 = \alpha\text{-OH}; R_2 = \alpha\text{-OH}$ (Cholate)
 $R_1 = \beta\text{-OH}; R_2 = H$ (Ursodeoxycholate)
 $R_1 = \alpha\text{-OH}; R_2 = H$ (Chenodeoxycholate)
 $R_1 = H; R_2 = \alpha\text{-OH}$ (Deoxycholate)
 $R_1 = \beta\text{-OH}; R_2 = \alpha\text{-OH}$ (Ursocholate)
 $R_1 = H; R_2 = H$ (Lithocholate)

$Y = \alpha\text{-O}$
 $Y = \beta\text{-O}$
 $Y = \alpha\text{-NH}$
 $Y = \beta\text{-NH}$
 $Z = OH$
 $Z = N\text{-CH}_2\text{CO}_2H$
 $Z = N\text{-CH}_2\text{SO}_3H$

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FIG. 9 *Uptake of (8) (XP10569) or Glycocholate by IBAT-Transfected CHO Cells*

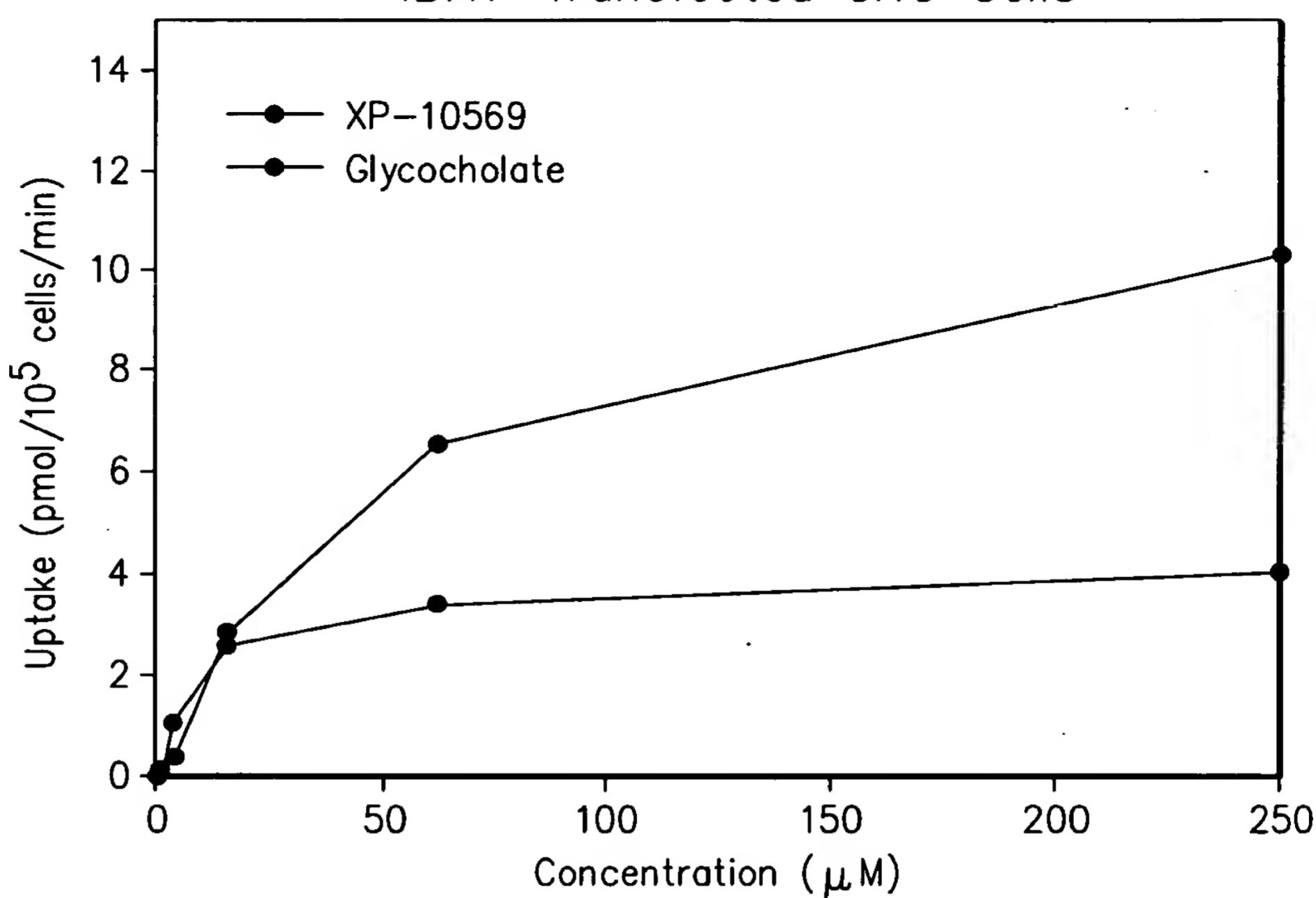
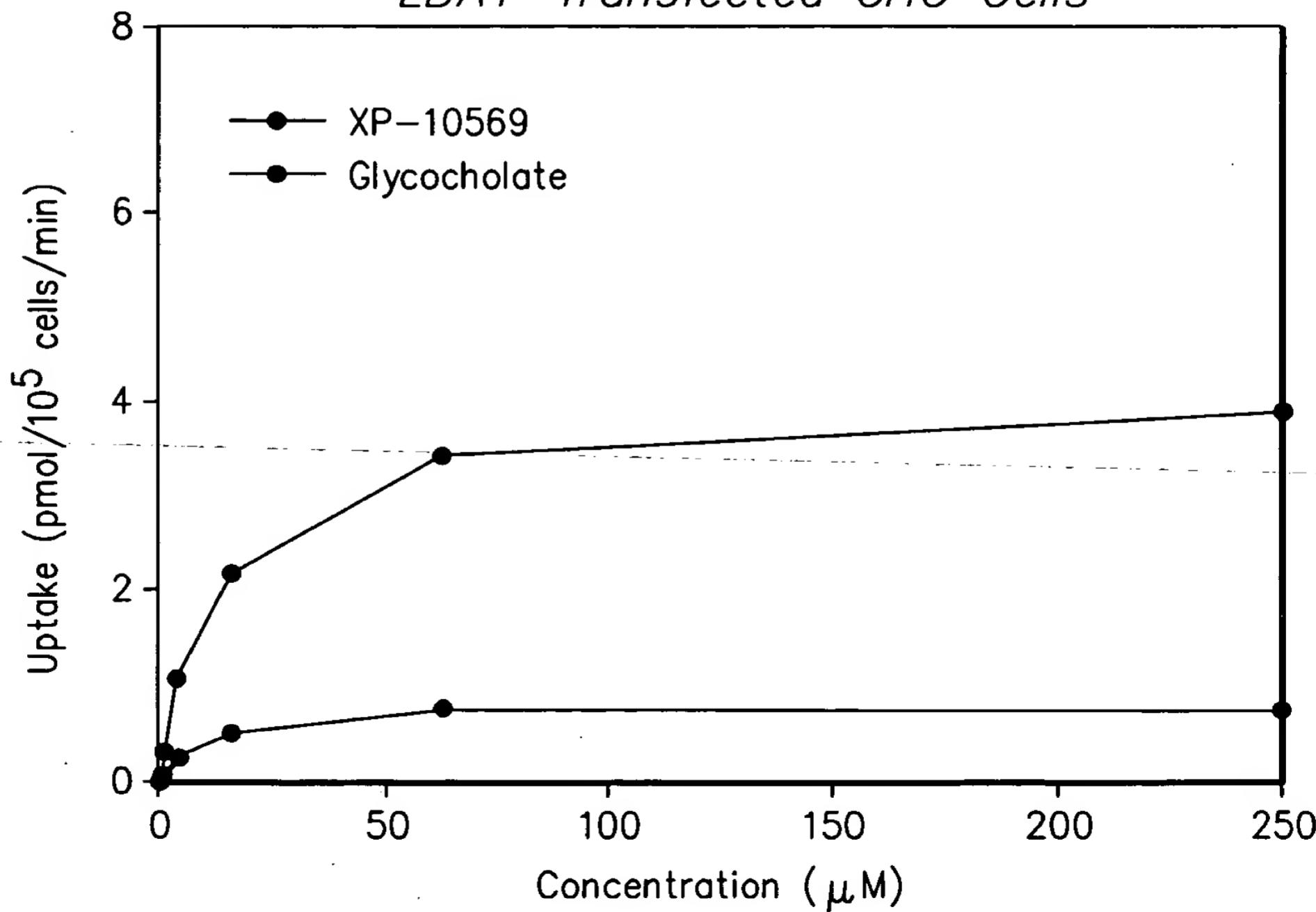
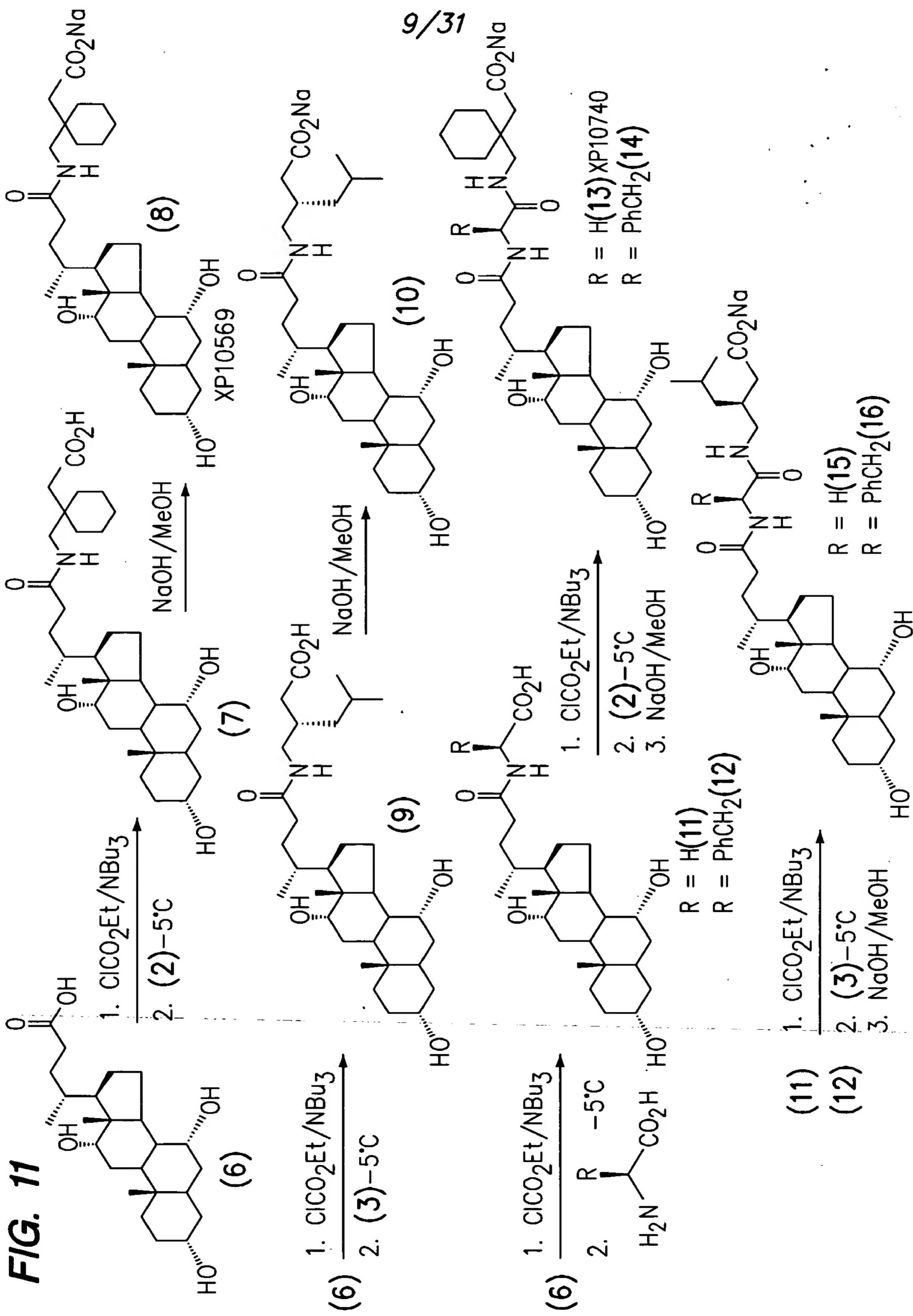


FIG. 10 *Uptake of (8) (XP10569) or Glycocholate by LBAT-Transfected CHO Cells*





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FIG. 12

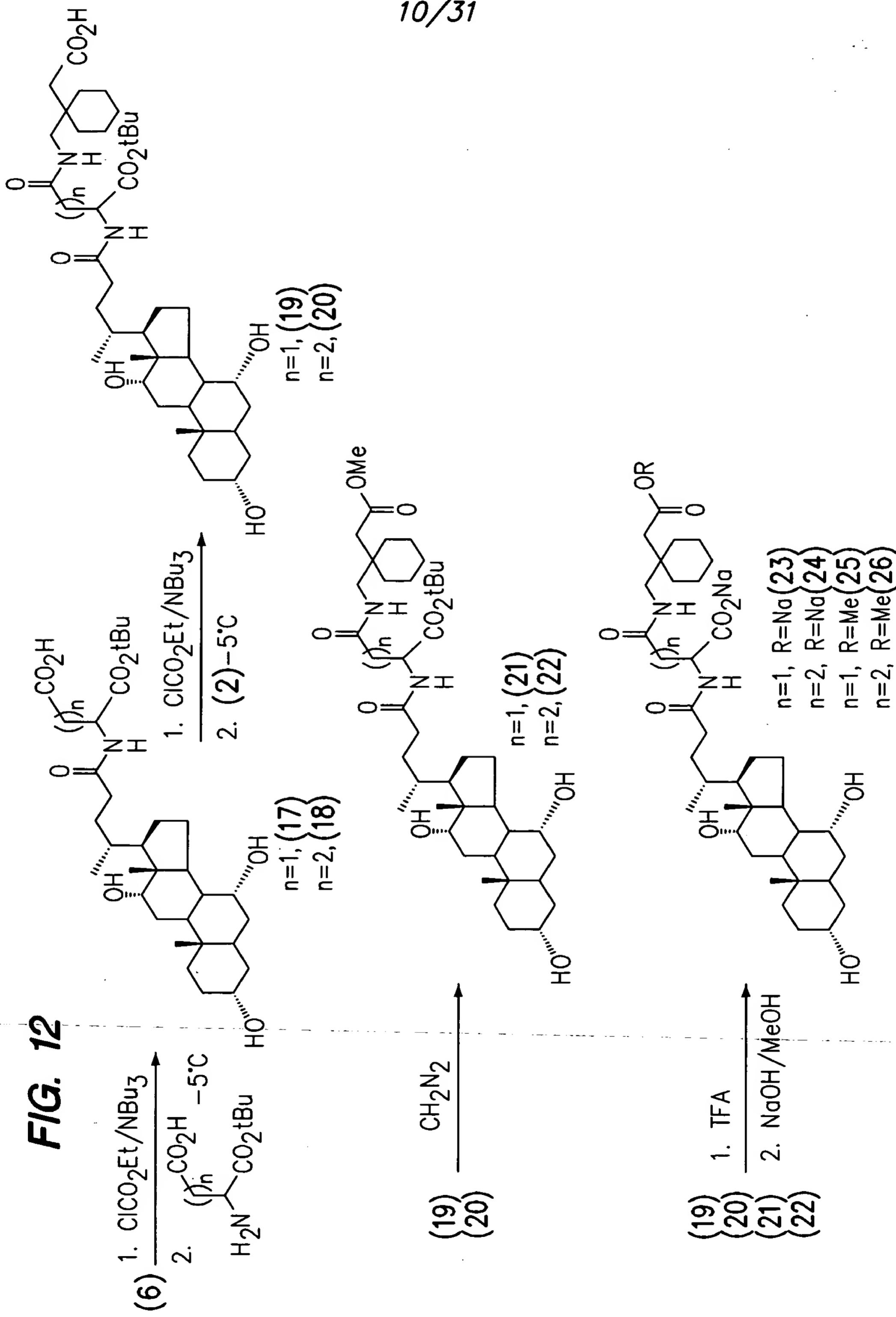
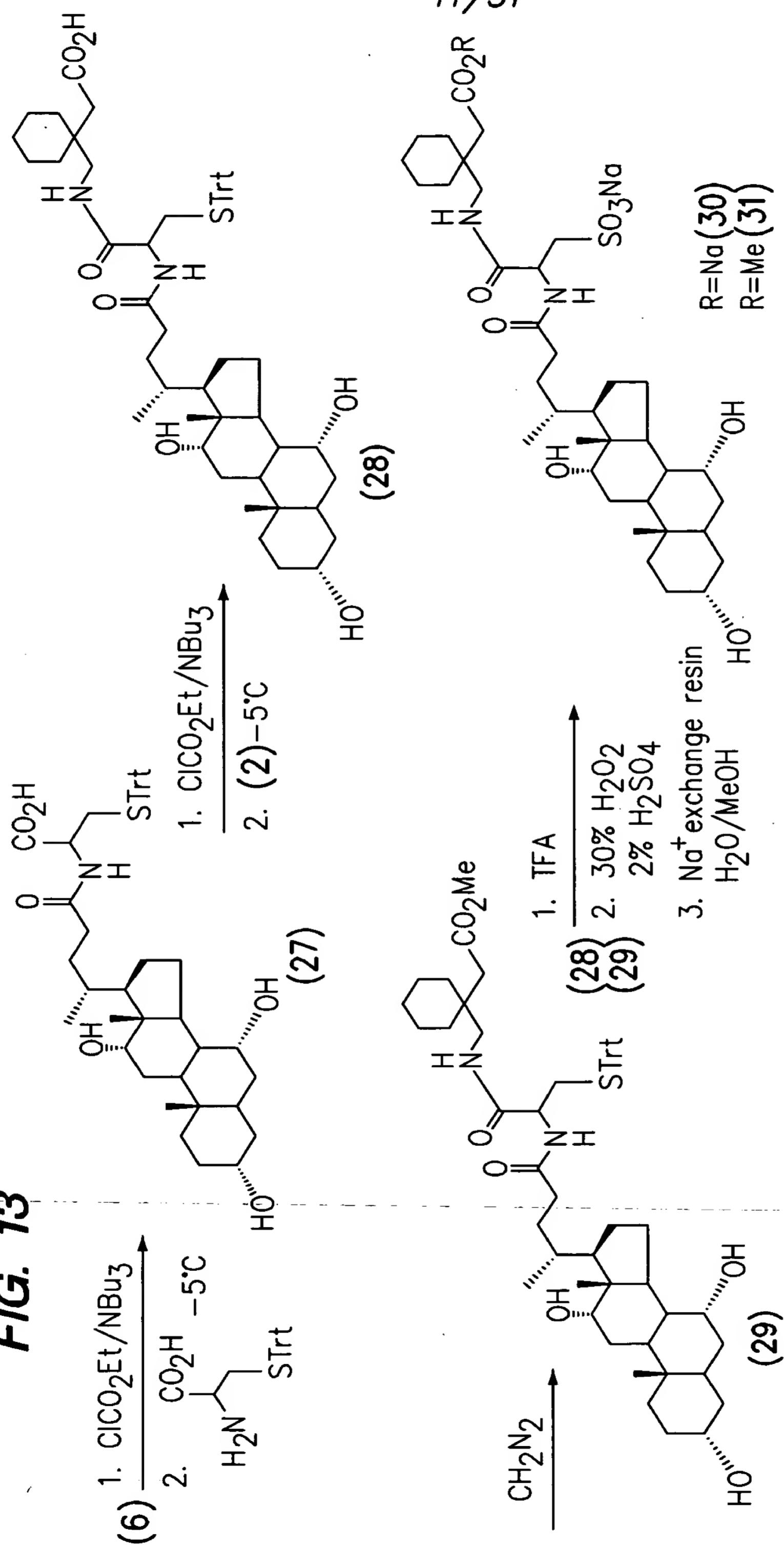


FIG. 13



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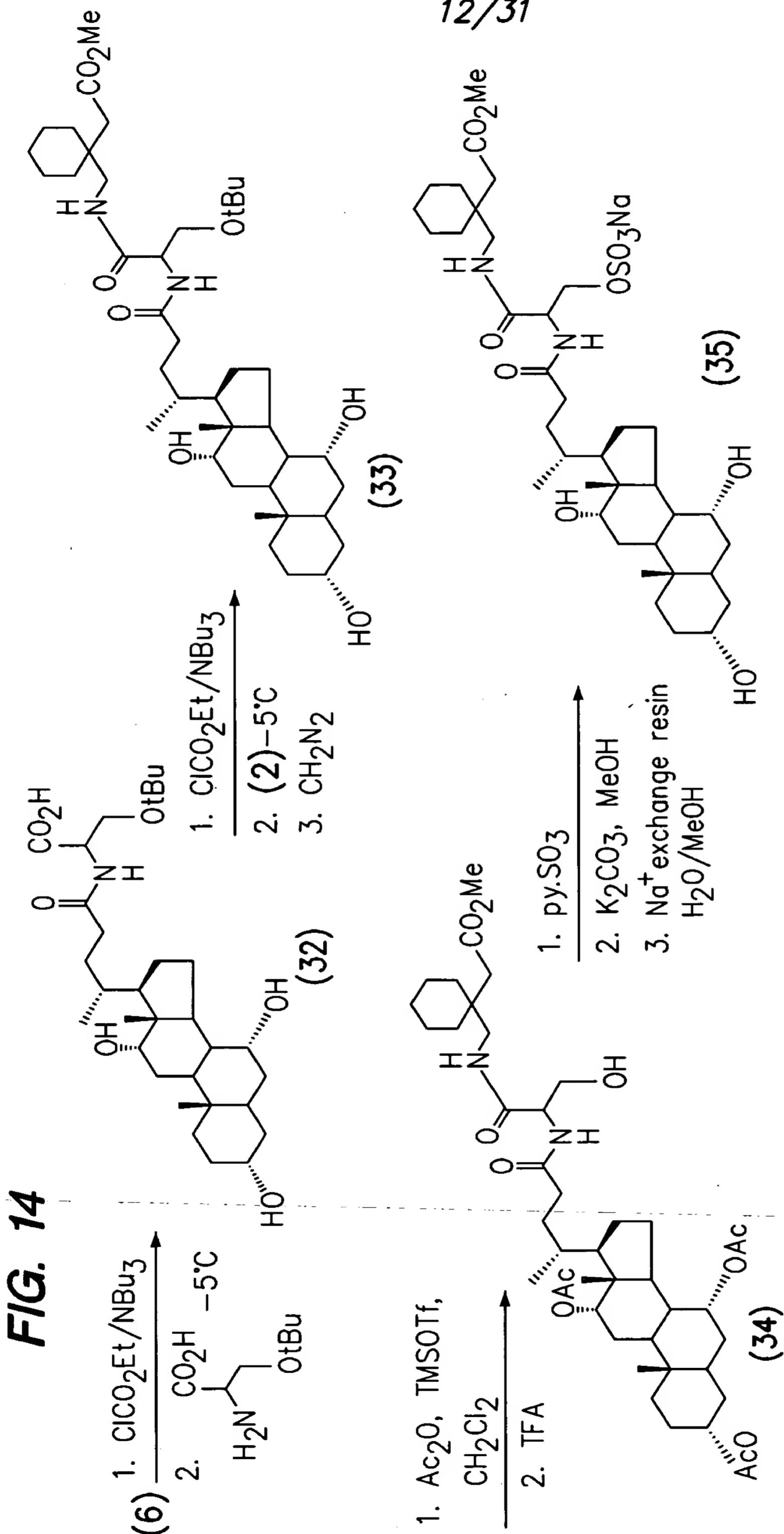
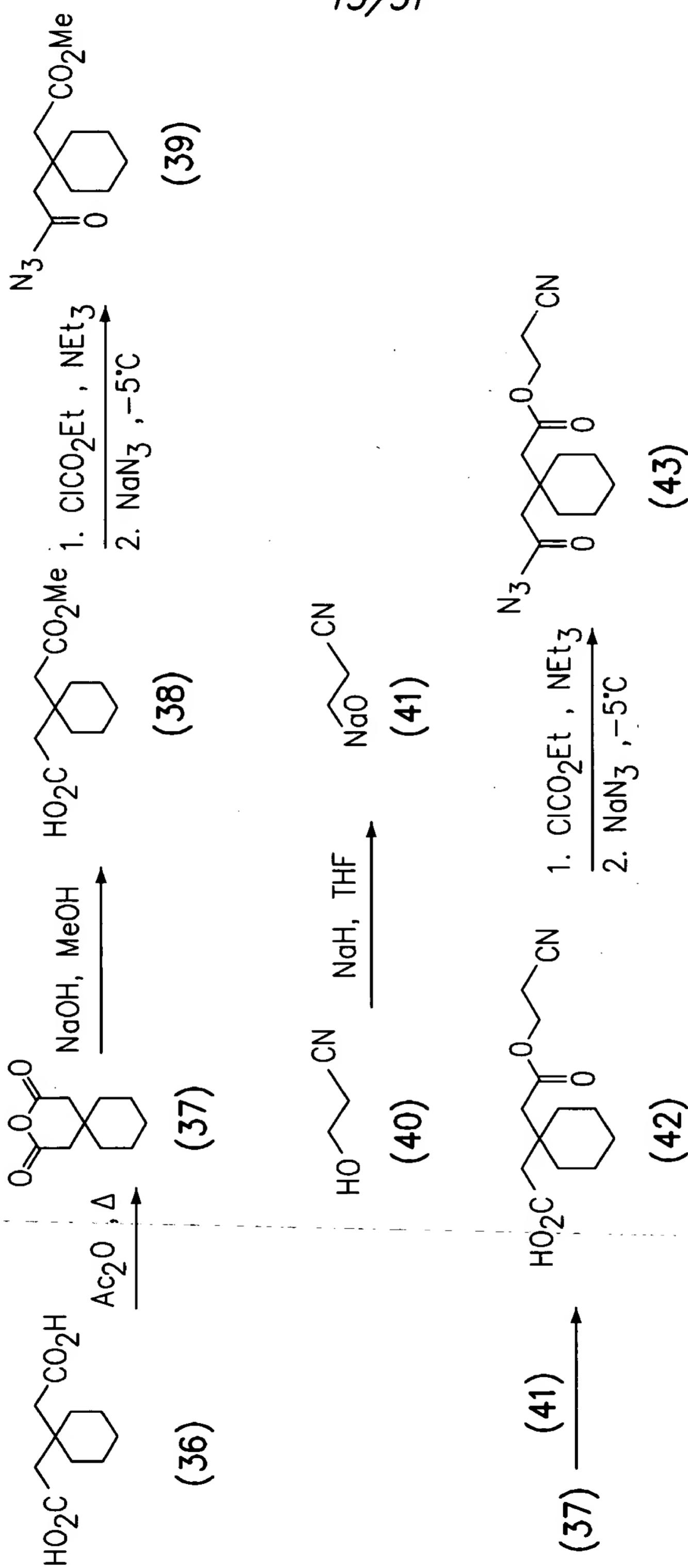


FIG. 14

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FIG. 15



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FIG. 16

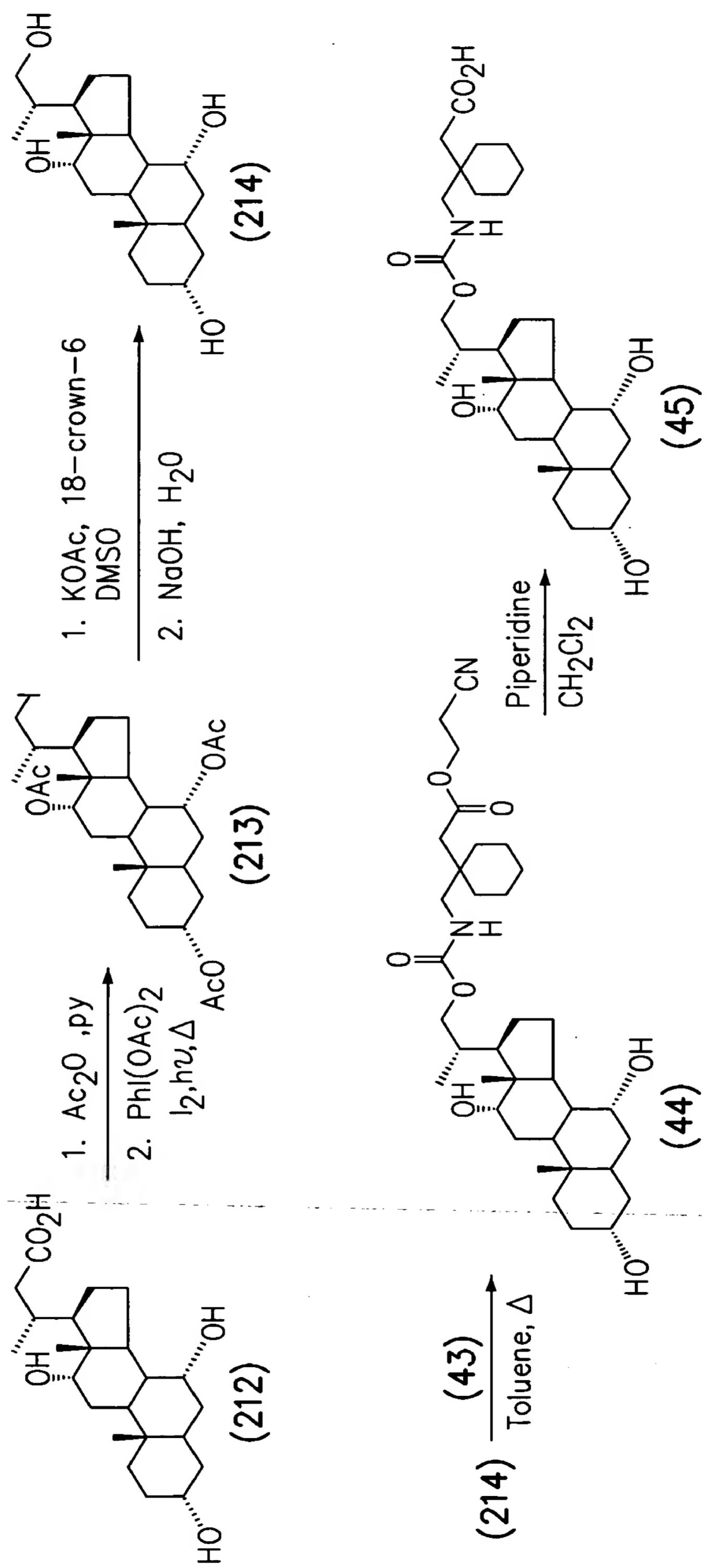
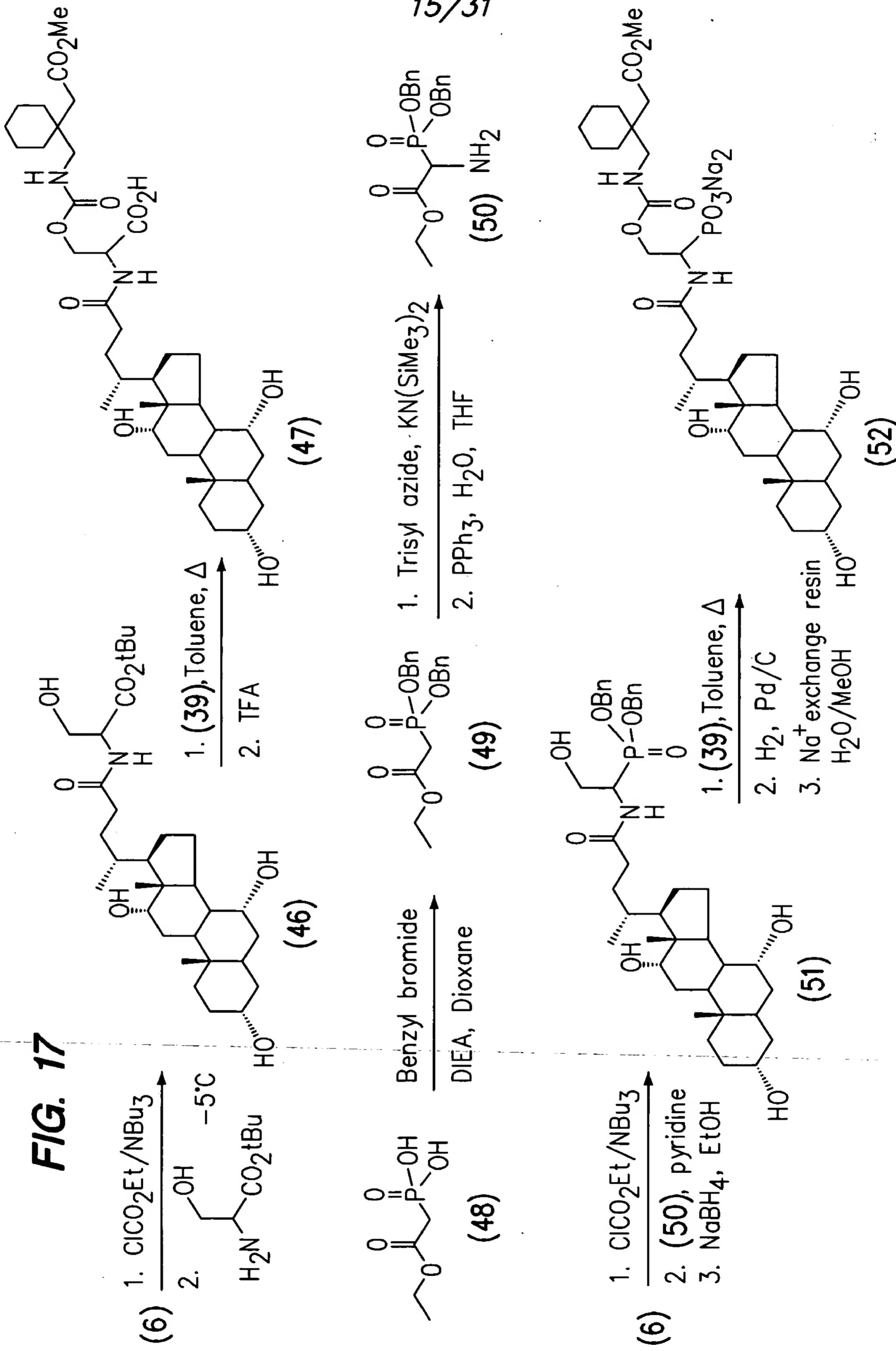
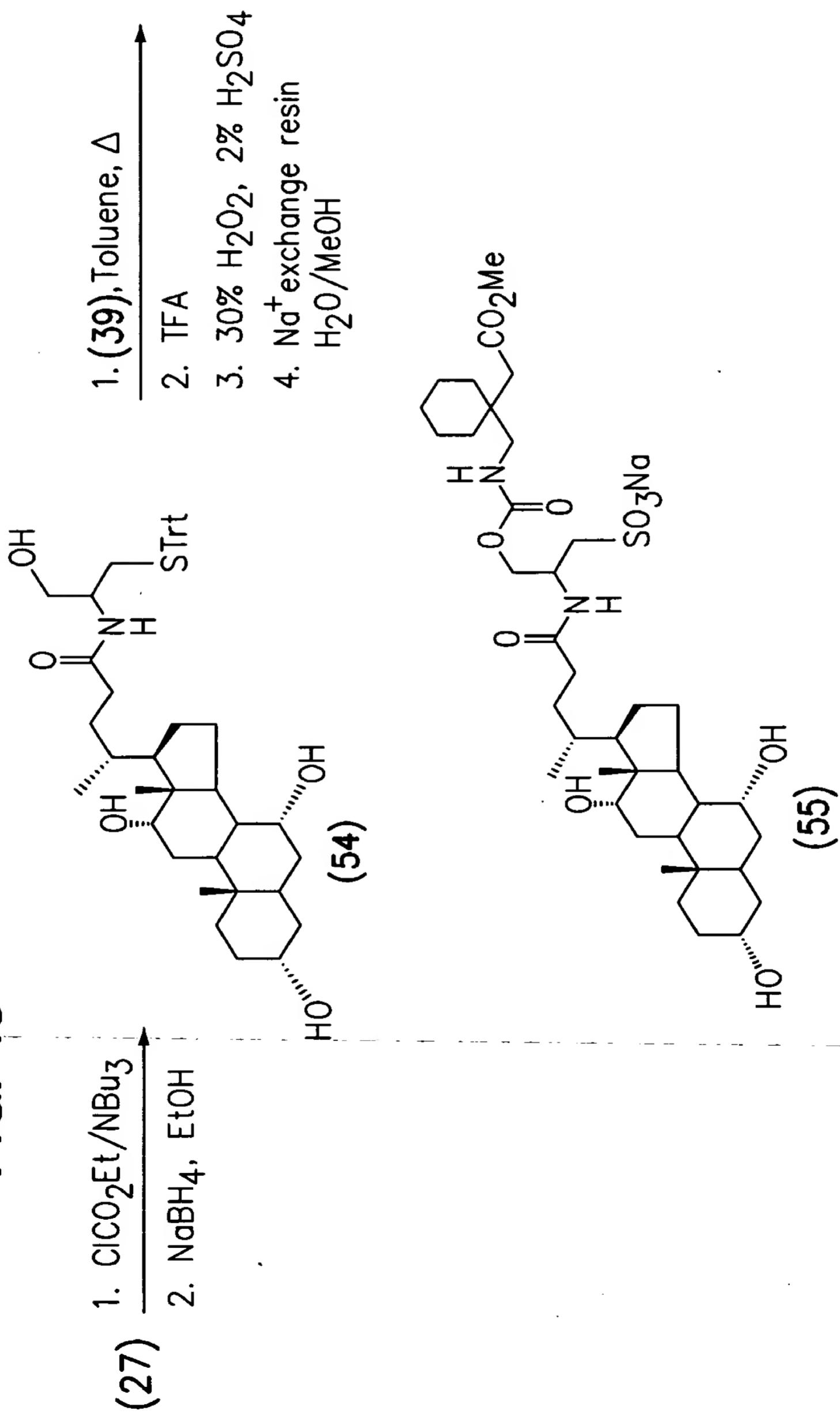


FIG. 17



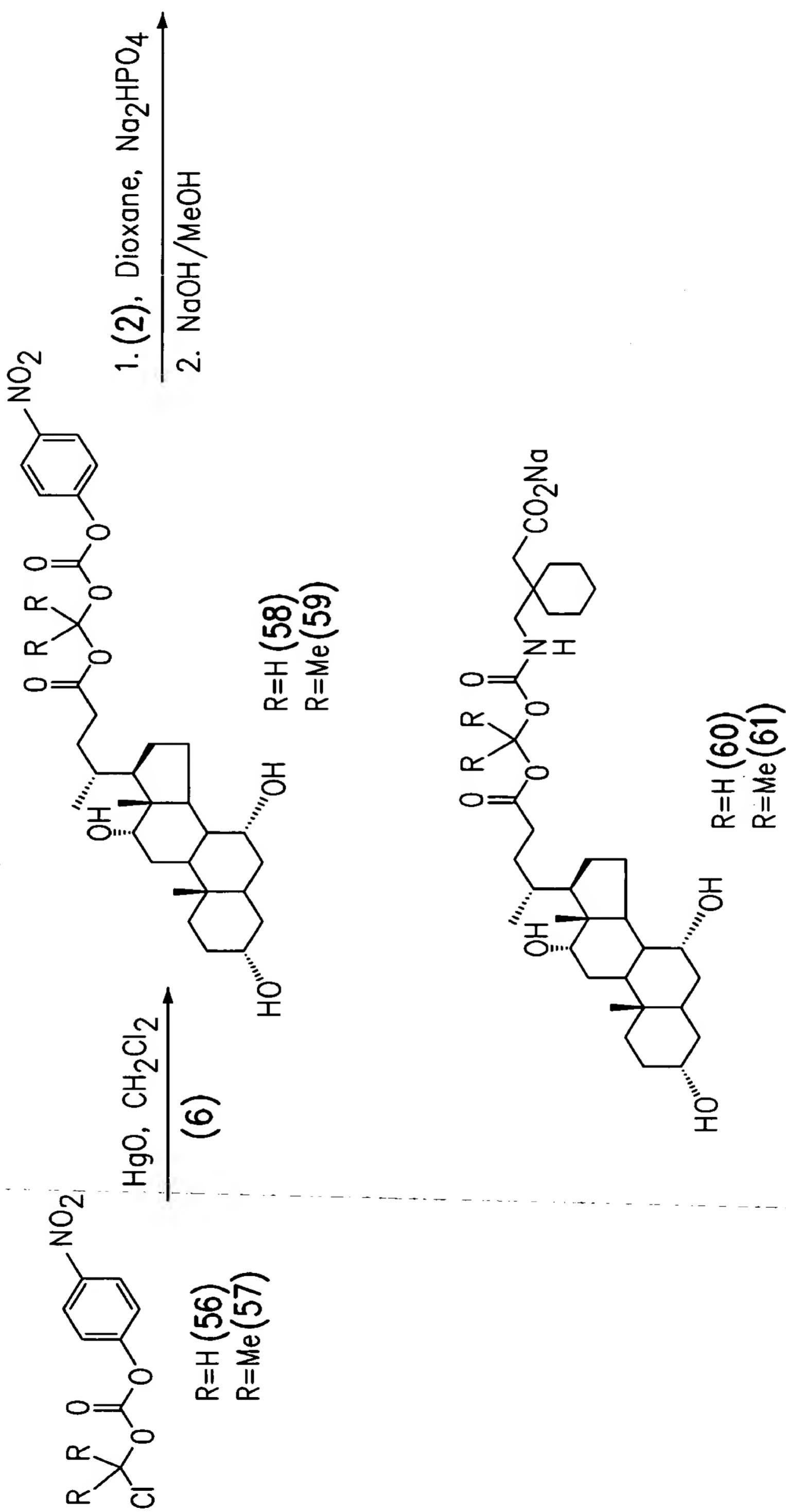
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FIG. 18



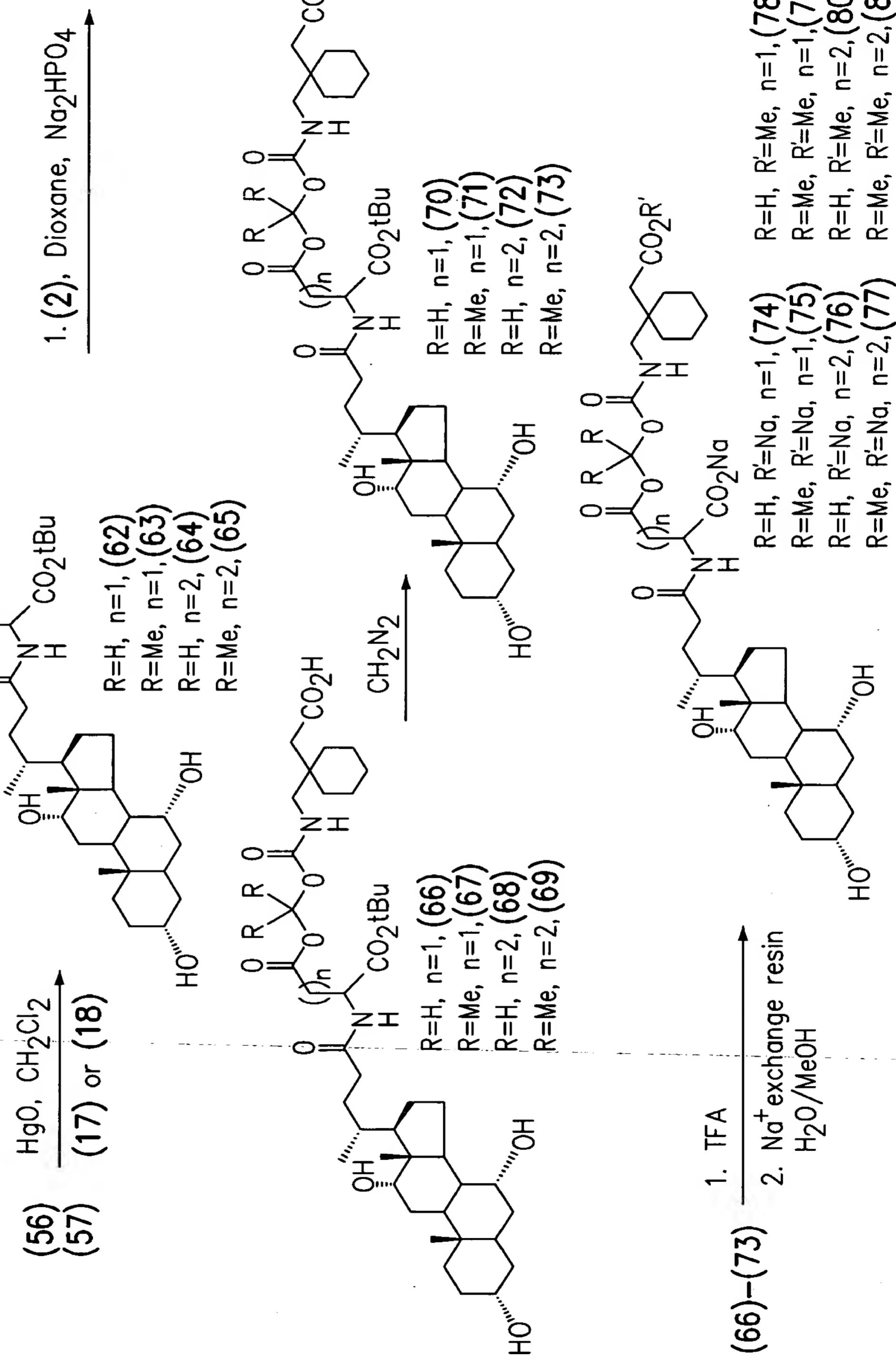
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FIG. 19

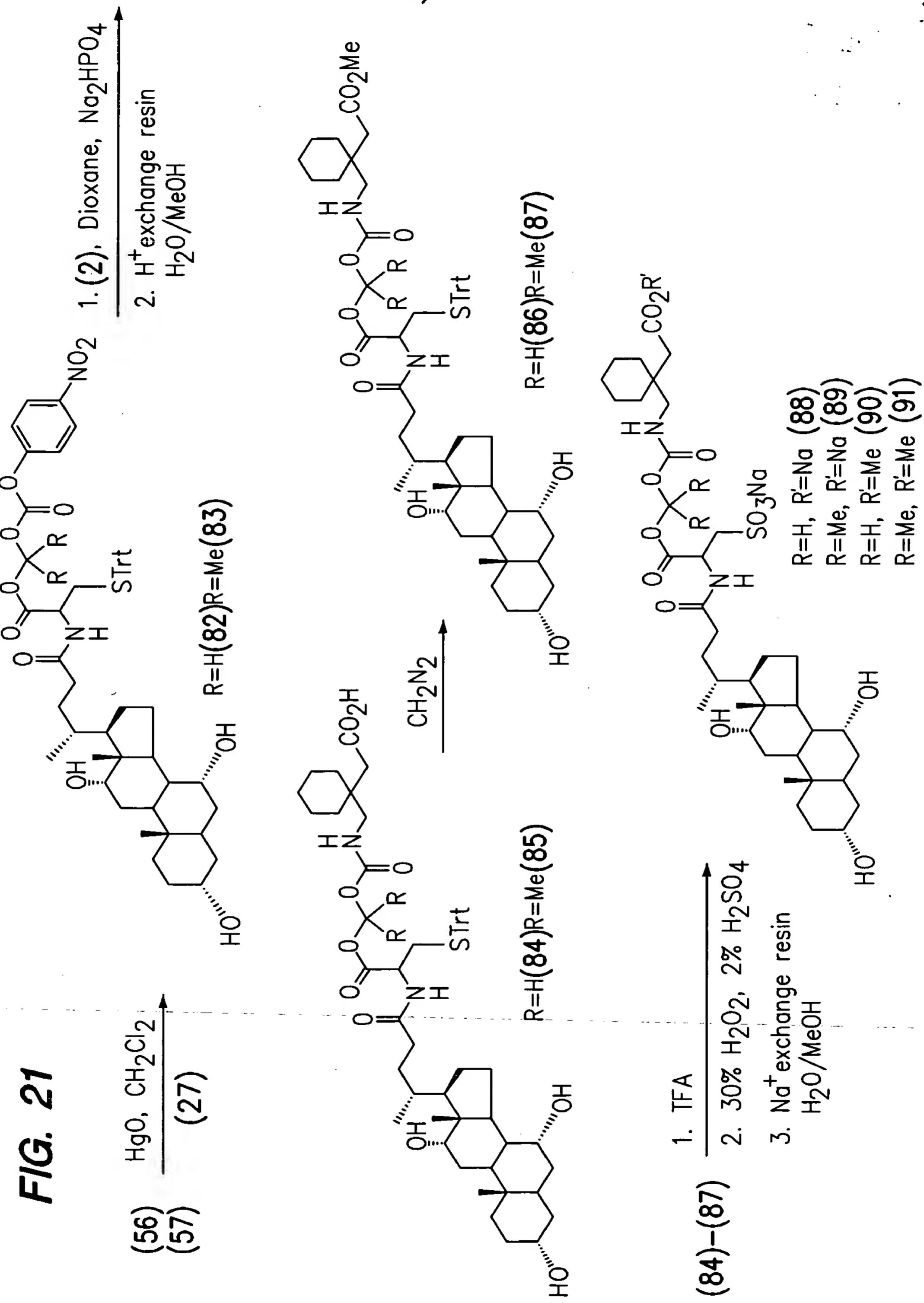


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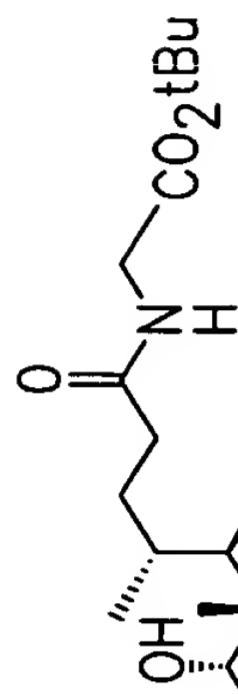
FIG. 20



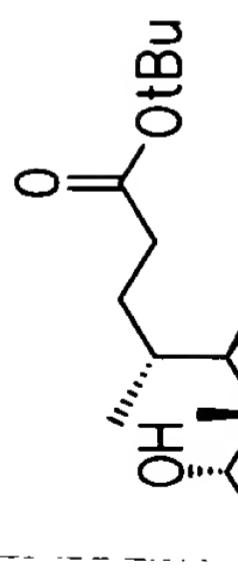
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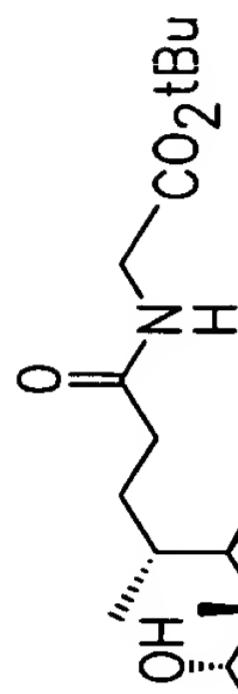
20/31



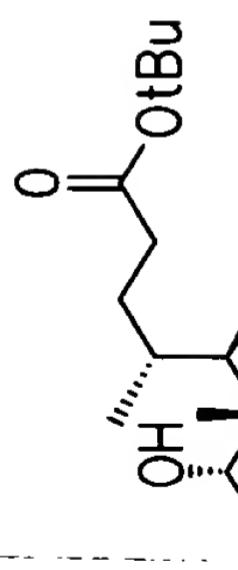
$\gamma = 3\alpha - 0 \{96\}$
 $\gamma = 3\beta - 0 \{97\}$
 $\gamma = 3\alpha - \text{NH} \{98\}$
 $\gamma = 3\beta - \text{NH} \{99\}$



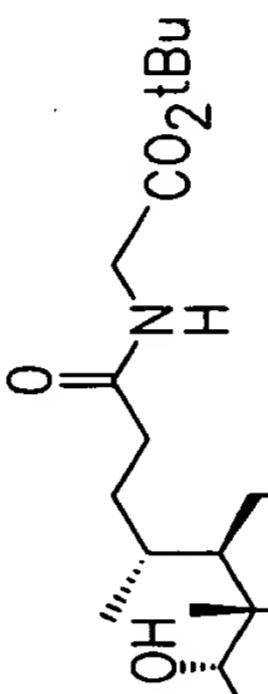
$\gamma = 3\alpha - 0 \{92\}$
 $\gamma = 3\beta - 0 \{93\}$
 $\gamma = 3\alpha - \text{NH} \{94\}$
 $\gamma = 3\beta - \text{NH} \{95\}$



$\gamma = 3\alpha - 0 \{96\}$
 $\gamma = 3\beta - 0 \{97\}$
 $\gamma = 3\alpha - \text{NH} \{98\}$
 $\gamma = 3\beta - \text{NH} \{99\}$

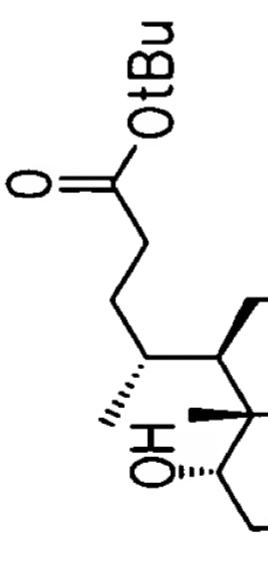


$\gamma = 3\alpha - 0 \{92\}$
 $\gamma = 3\beta - 0 \{93\}$
 $\gamma = 3\alpha - \text{NH} \{94\}$
 $\gamma = 3\beta - \text{NH} \{95\}$



$3\alpha - 0 \{102\}$
 $3\beta - 0 \{103\}$

$n = 1 - 5$



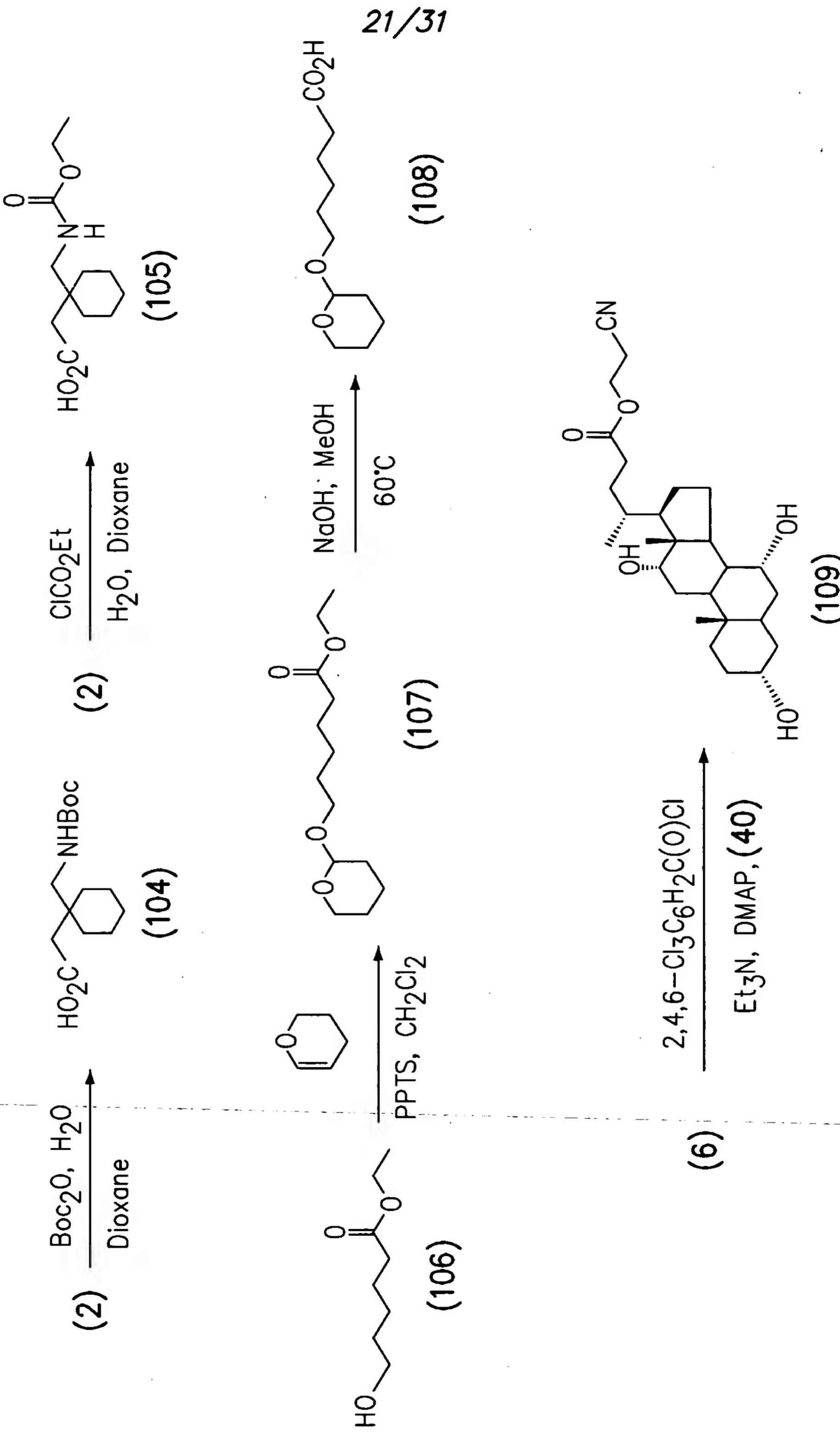
$3\alpha - 0 \{100\}$
 $3\beta - 0 \{101\}$

$n = 1 - 5$

FIG. 22

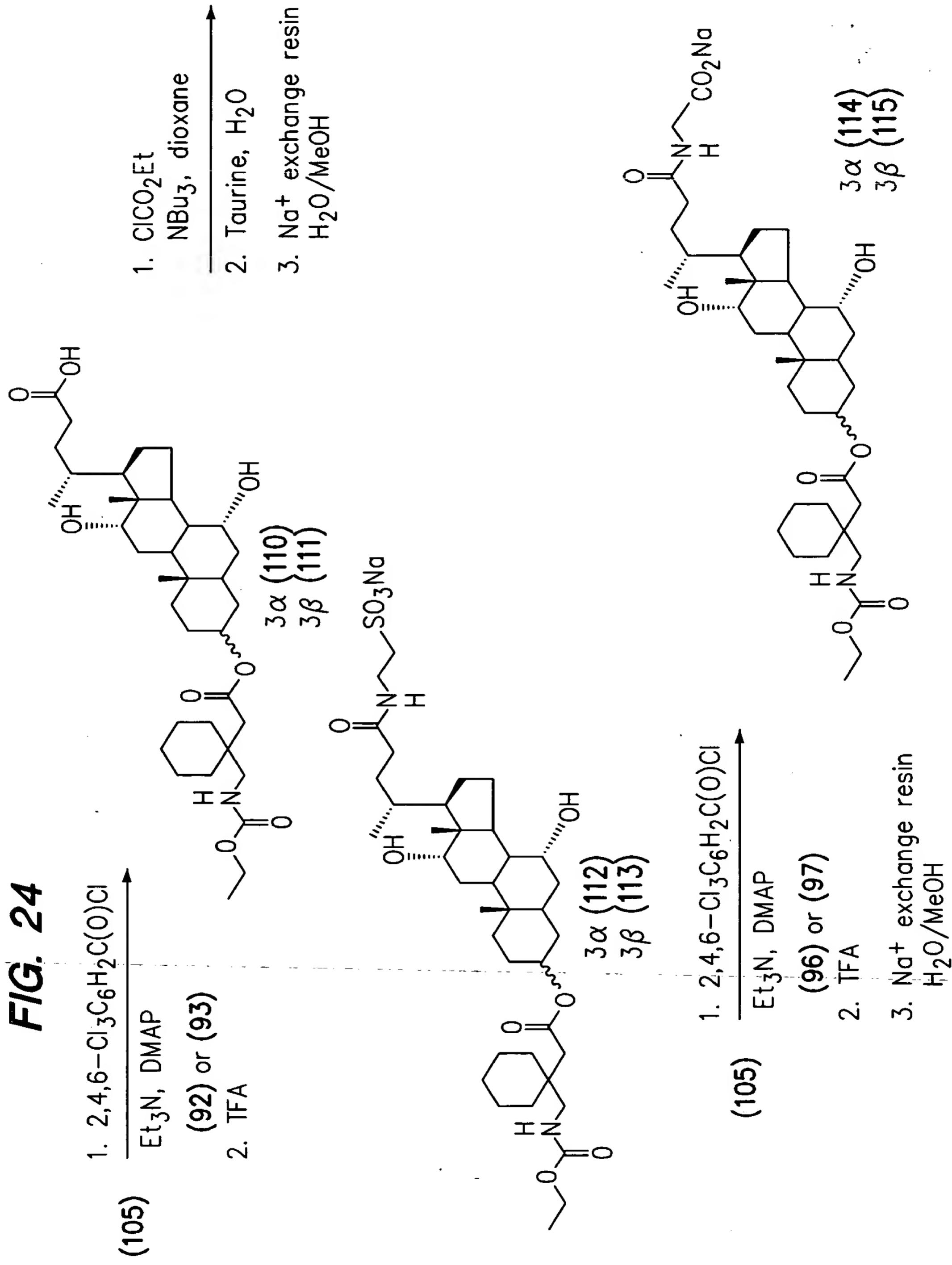
Compounds (92)-(103) prepared following methods described in co-pending application "Bile Acid-Derived Compounds for Enhancing Oral Absorption and Systemic Bioavailability of Drugs" assigned to XenoPort, Inc.

FIG. 23



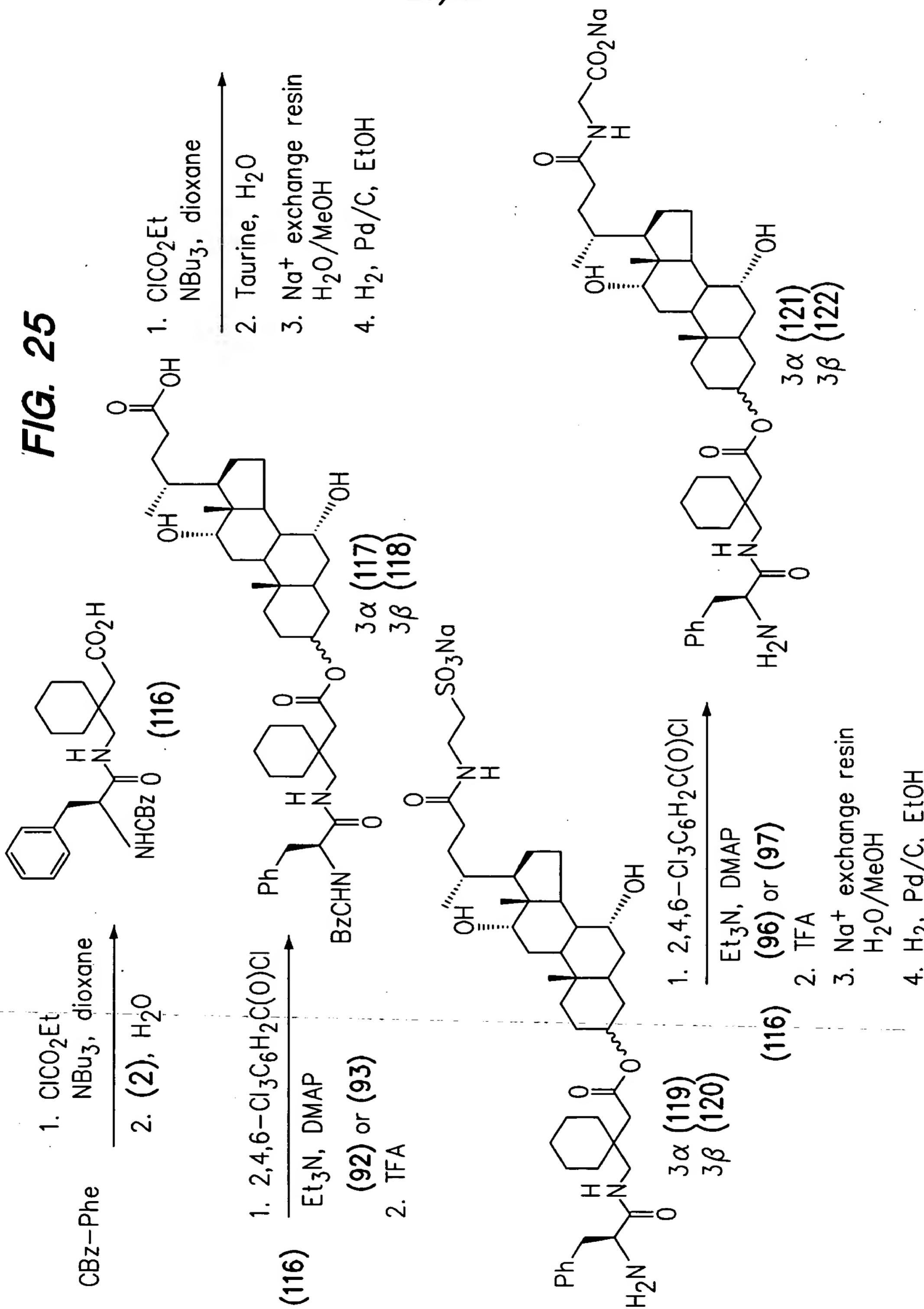
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FIG. 24

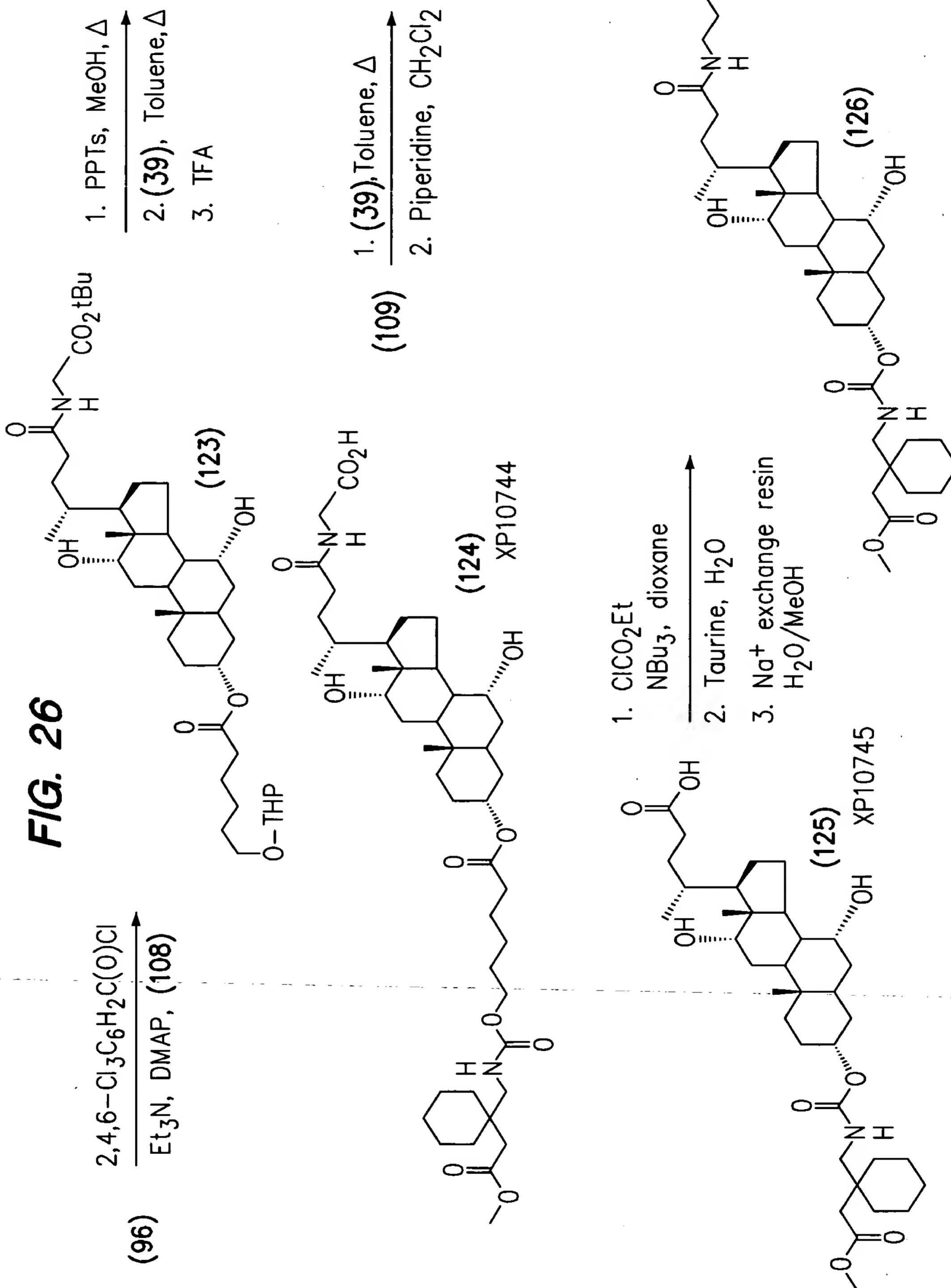


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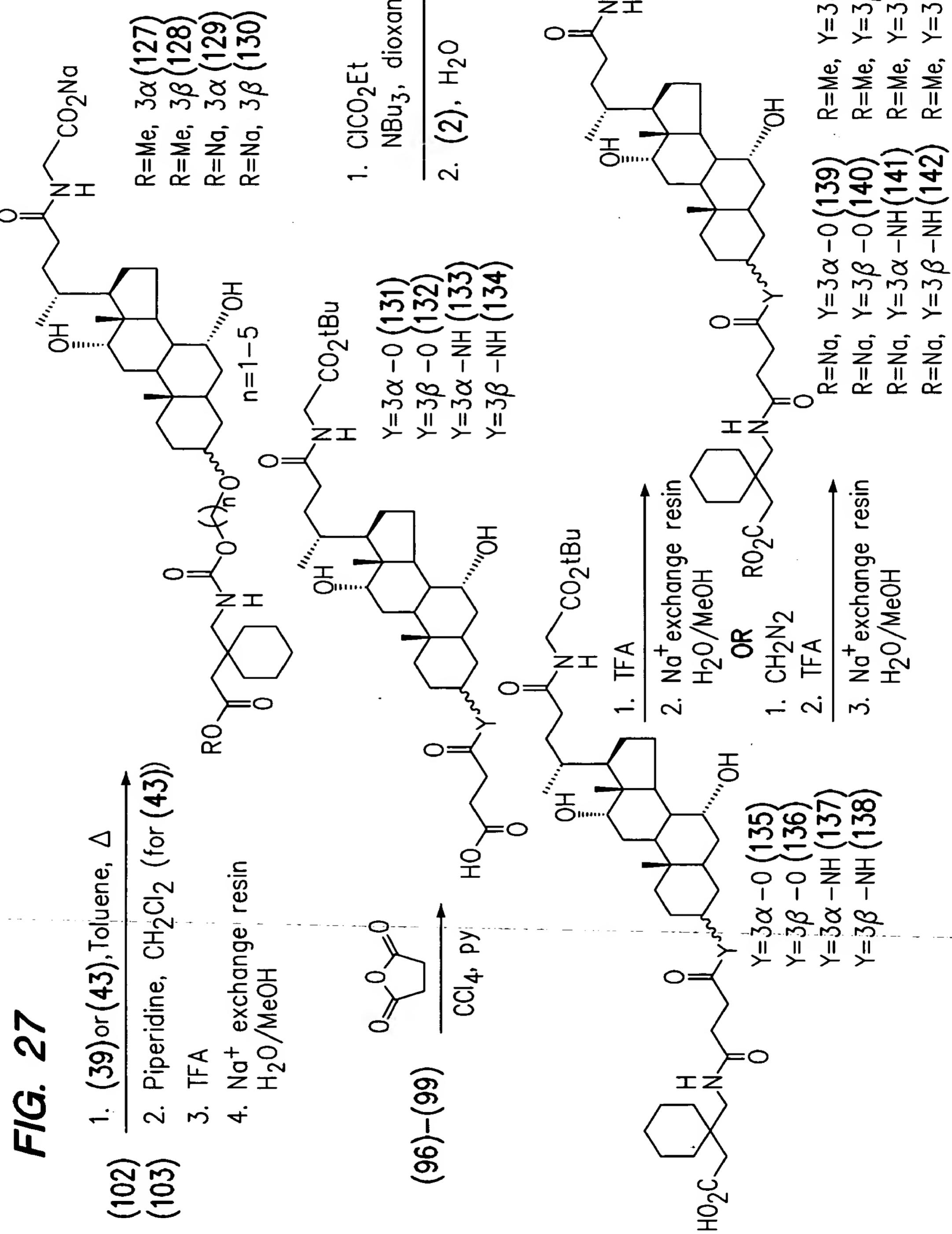
FIG. 25



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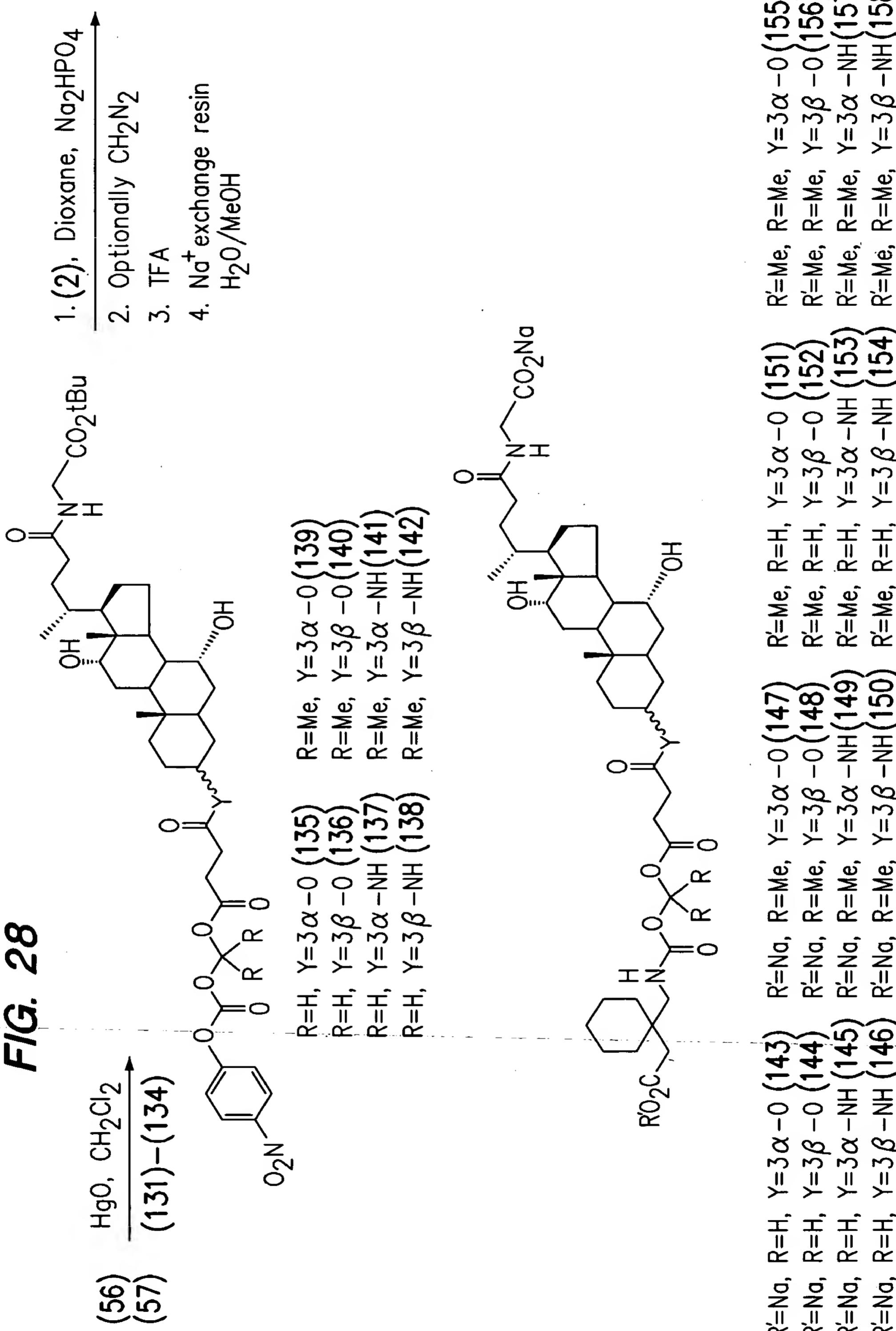


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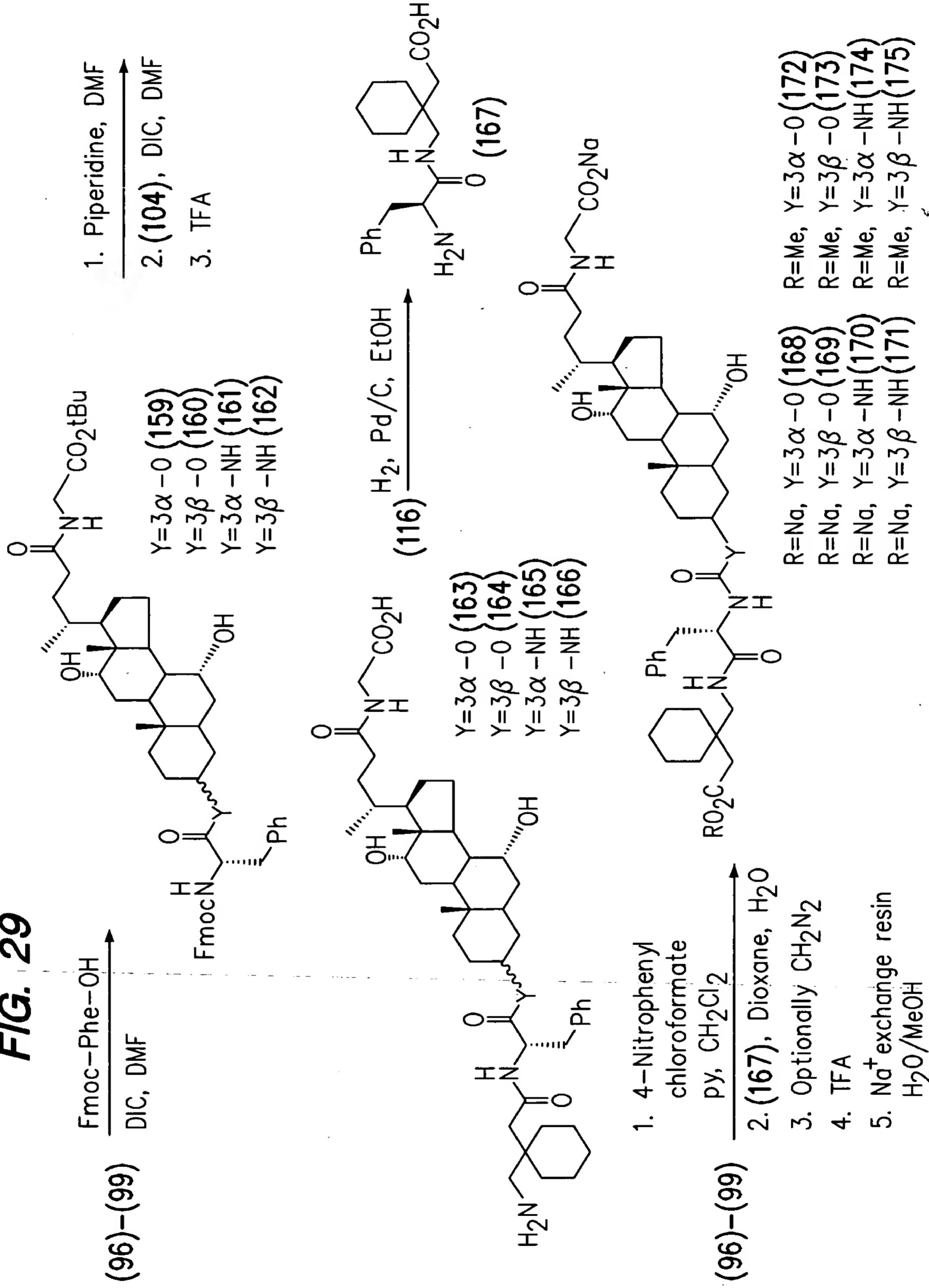
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FIG. 28

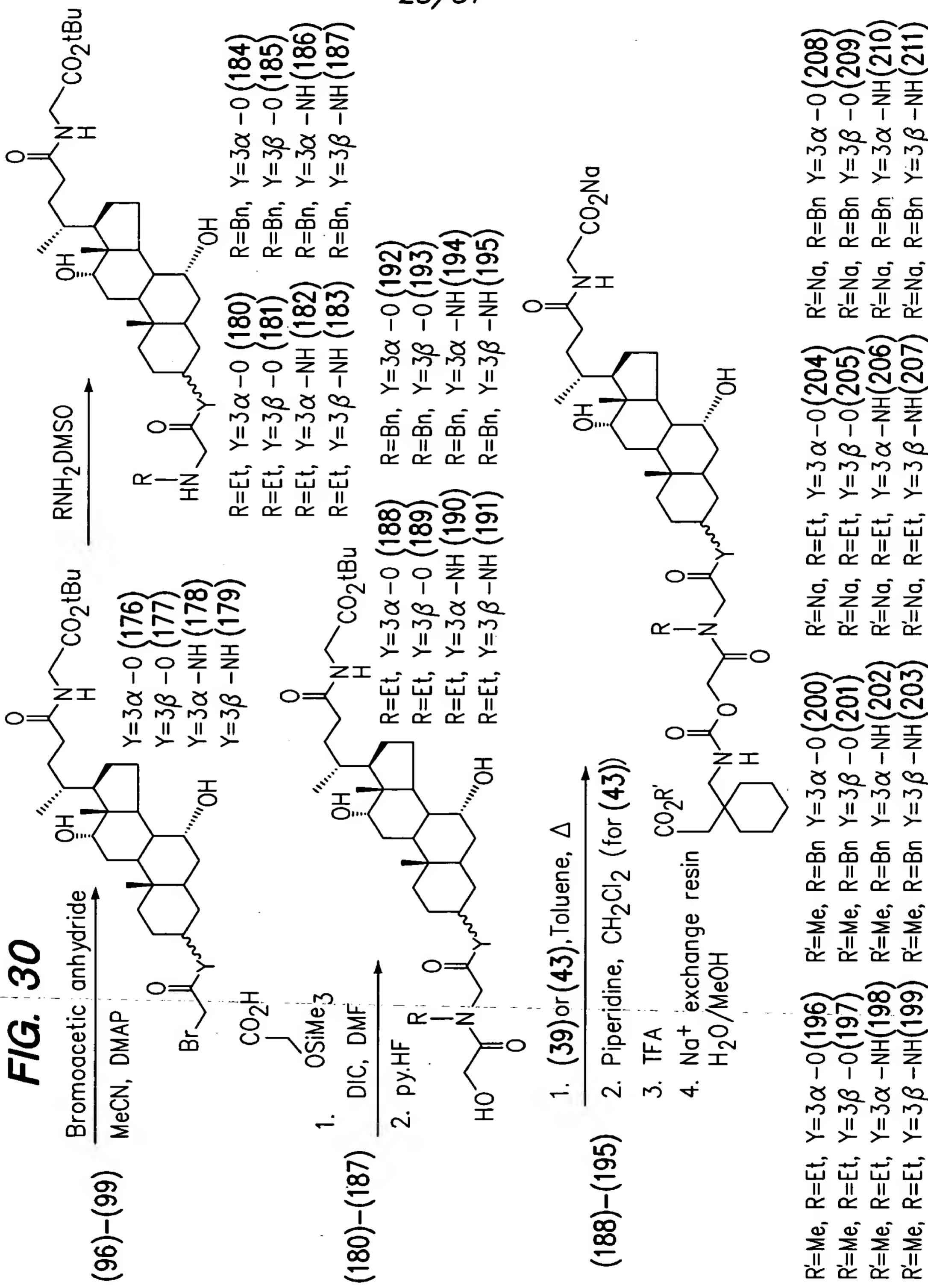


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FIG. 29



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FIG. 31

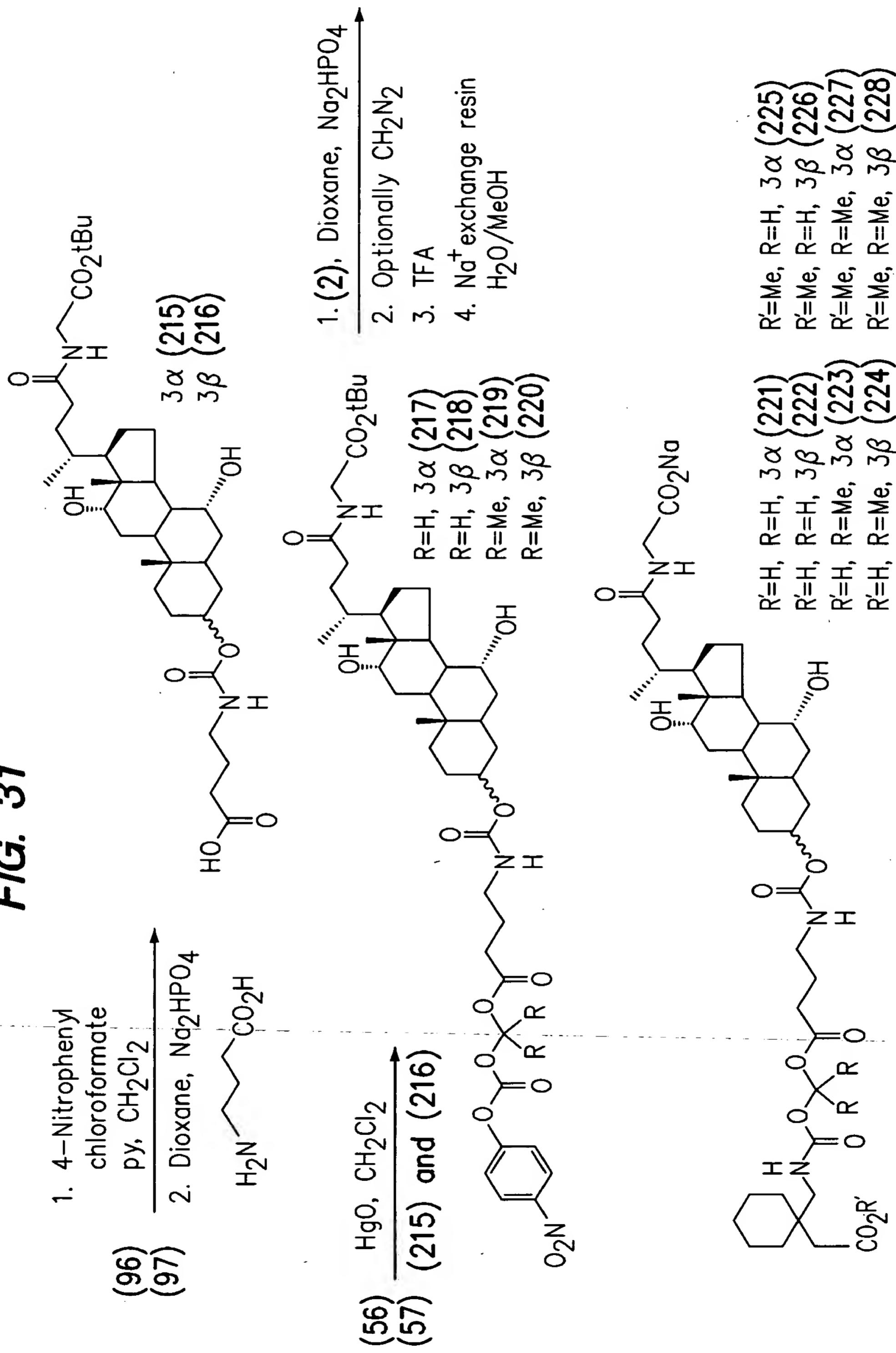
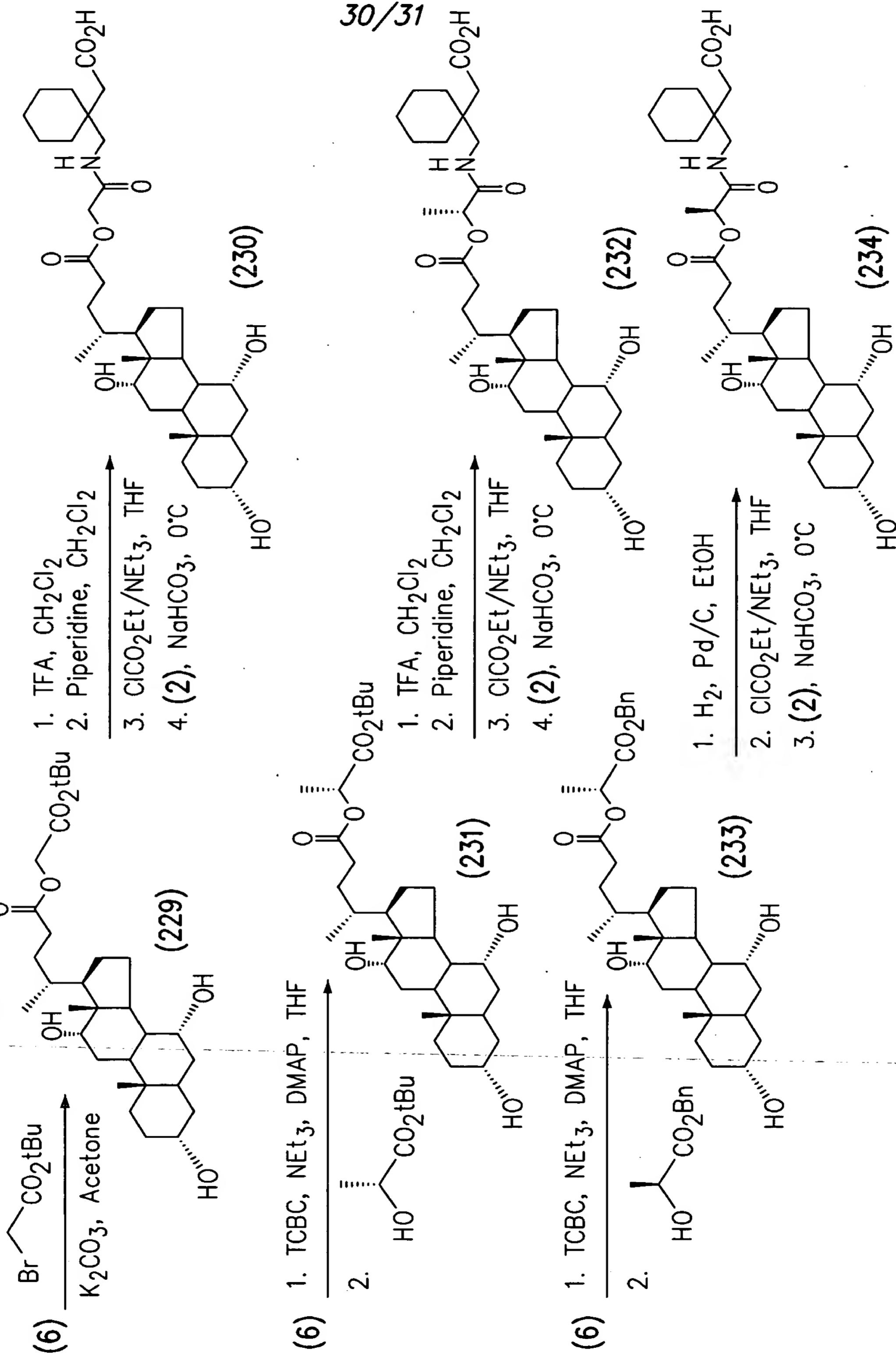


FIG. 32



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FIG. 33

